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***Observational Study***

**Neglected features of lifestyle: their relevance in non-alcoholic fatty liver disease**

Trovato FM *et al.* Neglected lifestyles in NAFLD

**Francesca M Trovato, Giuseppe Fabio Martines, Daniela Brischetto, Guglielmo Trovato, Daniela Catalano**

**Francesca M Trovato, Giuseppe Fabio Martines, Daniela Brischetto, Daniela Catalano,** Department of Clinical and Experimental Medicine, Postgraduate School of Clinical Echography, the University of Catania, 95100 Catania, Italy

**Guglielmo Trovato,**Clinical Research and Innovation Project Planning Unit, the School of Medicine and AOU Policlinico, the University of Catania, 95100 Catania, Italy

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**Correspondence to:** **Daniela Catalano, MD,** Department of Medicine, the School of Medicine of the University of Catania, Policlinico, Via Santa Sofia 78, 95100 Catania, Italy. [danielacatalano@unict.it](mailto:danielacatalano@unict.it)

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**Abstract**

***AIM***

To investigated in non-alcoholic-fatty-liver-disease (NAFLD), with ultrasound-detected fatty liver, and in a group of non-alcoholic and otherwise healthy subjects, relationship of neglected lifestyle with NAFLD and obesity.

***METHODS***

Five hundred and thirty-two NAFLD and 667 non-NAFLD healthy subjects, age 21-60 years were studied. Severity of liver steatosis was assessed by Ultrasound (US) Bright Liver Score (BLS). The Adherence to Mediterranean Diet profile Score (AMDS) was assessed on the basis of a 1-week recall computerized questionnaire which included a detailed physical activity reports (Baecke questionnaire). The Western Dietary Profile score, as a simplified paradigm of unhealthy diet, a questionnaire quantifying sun exposure score and a sleep habits questionnaires provided a further comprehensive lifestyle assessment.

***RESULTS***

Body mass Index (BMI), Insulin resistance (HOMA), and Triglycerides, poorer adherence to a Mediterranean Diet profile, sedentary habits, minor sun exposure and use of “western diet” foods are greater in NAFLD. Multiple Linear regression analysis, weighted by years of age, displays BMI, HOMA and AMDS as the most powerful independent predictors of fatty liver severity, however, also the physical activity score, the western diet habit and the sun exposure score are acting still inside the model with significant independent effects.

***CONCLUSION***

Articulated clinical intervention, according to our results, are justified in NAFLD and can be pursued addressing by focused intervention nutritional profile, physical exercise mainly in open-air subsets for enhancing sun exposure and healthier sleep duration and rhythm.

**Key words:** Fatty liver; Ultrasound; Diet; Malnutrition; Obesity; Health psychology; Sleep; Sun exposure; Clinical risk management

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**Core tip:** Non-alcoholic-fatty-liver-disease (NAFLD) is a multifactorial condition associated with malnutrition and, mainly, with obesity, sedentary life and insulin resistance; Some neglected factor, such as sleep and sun exposure curtailment, along with D vitamin deficiency, are associated with NAFLD; Articulated clinical intervention, according to our results, is justified in NAFLD and can be pursued addressing by focused intervention nutritional profile, open-air physical exercise for enhancing sun exposure and healthy behaviour targeted to improved sleep duration and rhythm.

Trovato FM, Martines GF, Brischetto D, Trovato G, Catalano D. Neglected lifestyles in non-alcoholic fatty liver disease. *World J Hepatol* 2016; In press

**INTRODUCTION**

Liver diseases, already in the past, were considered at least partly a consequence of unhealthy lifestyles and adverse environmental conditions, a concept that was very well addressed also by pathologists[1]. Lifestyle regards the use of the body functions related to physical exercise, exerted in work, love, leisure or sport, the quality and quantity of food, the sleep and rest rhythms, the exposure to hostile or unhealthy environmental factors, and other aspects, including fashion, clothing and non-sport leisure activity[2,3]. As in the past, the impact of the fashions and of beliefs based on alleged scientific statements and commercial information, namely publicity, is the key factor[4]. This framework, also by conditioning different lifestyles, reasonably affects the “establishment and maintenance of several diseases, including liver disease”[5]. In a very simplified manner today we tend to describe the lifestyles in medicine especially in terms of diet and physical inactivity or sedentary life, with a synergistic effect on body size – obesity – and on disease related with excessive food intake (atherosclerosis and liver disease)[6]. Marketing strategies focus much on some related aspects that have an influence on nutrition and physical activity, but also with trade repercussions, while neglecting and avoiding other modes of social behavior. Some of these factors, such as sleep duration[7,8], the sleeping patterns[9-12], including shift-work related effects[7], exposure to noise[13,14], the level of social alarm about events or situations[15], the possibility of urban mobility[16,17], may have determinant effects on nutritional profiles and exercise implementation. Communication and perception of risks, as traditionally recognized, are flanked by communication and induction of apparently neutral behavior that can behave as true risk factors for disease. The strong pressure towards practices aimed at optimizing physical fitness and dietary methods aimed at healthy foods often involves forms of orthorexia[18]; such strategies are widely used to gain and maintain niches of food and fitness markets. All this would be irrelevant, except that, as in the case of prevention of obesity and fatty liver, and probably also in the field of atherosclerotic, neurodegenerative and cancer diseases, dietary caloric intake and a sedentary lifestyle are not the only factors exerting independent synergistic effects[6]. In fact, even the dietary profiles[19], methods of exercise implementation[20,21], and other related factors, such as sleep deprivation[4], D vitamin deficiency and exposure to sunlight[22], environmental noise[16], and reasonably also others, seem to be part of an interrelated group of neglected risk factors, which only now are beginning to be studied more methodically.

Aim of our research is to investigate if some of the above mentioned neglected behavioural factors, concurrently with nutritional and physical exercise profile, may be associated or contribute independently as factors related to fatty liver in a group of non-alcoholic and otherwise healthy subjects with ultrasound-detected fatty liver.

**MATERIALS AND METHODS**

***Patients***

Five hundred thirty-two NAFLD and 667 non-NAFLD subjects (women 749, men 450, total 1199), age 21-60 years, without relevant acute or chronic disease, as below detailed in the exclusion criteria, were studied. These patients were consecutively referred to the same out-patients public medical unit (day-hospital) for lifestyle-nutritional prescription addressed to the management of minor digestive disease (mainly gastro-esophageal reflux syndrome or irritable bowel syndrome), overweight or obesity. The subjects were enrolled throughout January 2008-December 2015, were all patients first-time visitors, had not had previous referral or intervention in our unit, and were studied by a comprehensive ultrasound assessment (liver-abdomen, heart, thyroid and lung), according to our current practice[3]. Exclusion criteria: (1) all patients with signs of moderate-severe congestive heart failure, previous myocardial infarction, idiopatic myocardiopathy, pericarditis, malignancies; (2) severe chronic liver disease, apart from the lone finding of bright liver; abnormal aminotransferase levels at the beginning of this study, defined as alanine transaminase (ALT) > 30 IU/L in men and ALT > 19 IU/L in women; acute or chronic virus hepatitis, which were excluded by concurrent laboratory assays, as below detailed; (3) any history of diabetes mellitus (fasting glucose ≥ 126 mg/dL or HbA1c ≥ 6.5%) or drug intake of anti-diabetic drugs, particularly metformin; (4) extreme obesity (BMI ≥ 40) and underweight bad-nourished profile (BMI < 18.5 or serum albumin < 3g/dL); (5) acute and/or chronic infectious, rheumatic or autoimmune disease; and (6) alcohol abuse (exceeding 20 g/d on a weekly base); renal insufficiency, *i.e.,* glomerular filtration rate (eGFR) < 90 mL/min/ 1.73 m2 and/or proteinuria > 0.10 g/d. According to these exclusion criteria 1508 further subjects, potentially but only partially eligible, are excluded by this study.

***Laboratory/imaging methods***

The severity of liver steatosis was assessed by Ultrasound (US) Bright Liver Score (BLS), graded 1-3: grade 0 was the absence of bright liver, *i.e.,* a normal pattern[23] , BLS was and previously validated by US-guided FNAB (Fine needle aspirate biopsy by 20 Gauge Menghini’s needles)[3]; GE echo color Doppler machines (GE Logiq 5/Vivid7 Expert US manufactured by GE Medical Systems, Milwaukee, WI, United States), high resolution, equipped with real-time convex, phased array and linear scan transducers, were used throughout this study.

Routine laboratory tests included virus hepatitis (hepatitis A, B and C virus , i.e. HAV, HBV, and HCV) and cancer biomarkers (Alpha-fetoprotein, CEA, Ca125, Ca 19-9, Ca15-3), thyroid hormones FT3 FT4, thyroid-stimulating hormone (TSH), aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyl transpeptidase (γGT), ferritin, total protein, and albumin. Mediterranean Diet Adherence Profile was assessed by the Adherence to Mediterranean Diet Score (AMDS) on the basis of a 1-week recall computerized questionnaire[3,5] using a pictogram-based method of visualizing dietary intake, descriptive also of the size of the single portion; pictograms includes also items for the quantification of physical activity, which is otherwise quantified by detailed physical activity reports (Baecke questionnaire)[5]. The Western Dietary Profile score, as a simplified paradigm of unhealthy diet, was assessed submitting a specific questionnaire, which is reported in Appendix; also the Baecke’s physical activity questionnaire is briefly described in appendix, and subsequently the total score was studied by statistical analysis. The questionnaires submitted for quantifying sun exposure score, used mainly as an index of the open air activity and sleep habits questionnaires are routinely included within the context of a comprehensive lifestyle assessment, and detailed in appendix. The study and the manuscript were approved by the Institutional Review Board of the Project Office. No conflict of interest is to be declared for this invited manuscript. Written informed consent was obtained from each patient prior to the clinical data recording and before the US procedure, allowing the use of information for teaching and clinical research. Detail that might disclose the identity of the subjects under study is carefully omitted in any part of the study.

***Statistical analysis***

Comparison of data between the two groups of patients, NAFLD *vs* controls, is reported and differences assessed by Student’s t test. Subsequently: (1) ROC curve analysis of data of controls *vs* NAFLD subjects is used for defining the optimal cut-offs which may distinct the two group. The performance of each measure in prediction of NAFLD was evaluated by receiver operating characteristic (ROC) curve. The area under the ROC curve (AUROC) and the 95% confidence interval (CI) were used as indexes of accuracy. The optimal cut-off value was determined with maximum sum of sensitivity and specificity. For the purpose of identifying such thresholds, the measures used were BMI, HOMA, Mediterranean Diet Adherence Score (AMDS), Western Diet Score (WDS), Physical Activity Baecke’s total score, sun exposure score, and sleep daily hours, calculated on a weekly base; (2) contingency tables and Odds ratio of NAFLS vs. non-NAFLD were calculated, according to each defined cut-off; and (3) MLR analysis, weighted by age, using BMI, HOMA, Mediterranean Diet Adherence score, Western Diet Score, Physical Activity Baecke’s total score, Sun exposure score, sleep hours vs. BLS score of fatty liver was at last performed.

**RESULTS**

The two groups of patients were comparable for age (Table 1), while other measures, such as BMI, HOMA and Triglycerides are greater in NAFLD. Comparison of data between the two groups of patients, NAFLD vs. controls, is reported in detail (Table 1): a poorer adherence to a Mediterranean Diet profile, greater sedentary habits and greater use of “western diet” foods are the main differences. Moreover, liver size and, obviously, detection of fatty liver are the main ultrasound feature distinctive of the two groups.The ROC curve analysis graph of the data of controls vs. NAFLD subjects for BMI, HOMA, HDL Cholesterol is displayed in Figure 1.

The most suitable thresholds distinctive of NAFLD vs controls are, in our population: BMI ≥ 26.40, HOMA ≥ 1.87, HDL < 54.50, TGL≥ 94, Mediterranean Diet Adherence Score (AMDS) AMDS < 34, Western Diet Score (WDS) WDS ≥ 15.5, Physical Activity Baecke’s total score < 41.5, Sun exposure score SES < 34.5, and sleep daily hours, calculated on a weekly base Sleep Hours < 8.0. Contingency tables and Odds ratio were calculated for NAFLD vs. controls, according to above defined thresholds. Greater prevalence of overweight-obesity, insulin resistance, increased triglycerides and low HDL cholesterol, poor adherence to Mediterranean Diet Profile, greater use of Western diet food, greater sedentary life habits and minor sun exposure, open air time were observed (Table 2).

Multiple Linear regression analysis (Table 3), weighted by years of age for avoiding age as a potential confounding factor, using the same items as predictors of the severity of fatty liver, assessed by ultrasound as BLS, confirms the significance of the chosen model, displaying BMI, HOMA and AMDS as the most powerful predictors of fatty liver severity; also the physical activity score, the western diet habit and the sun exposure score are still inside the model, with significant independent effects. The number of sleep hours does not show any significant linear effect in the model. Nonetheless, in a separate analysis, sleep hours display a U shaped behaviour, showing a greater relationship with more severe fatty liver at the two extremes of the curve: few and many hours of sleep are both associated with more severe fatty liver.

DISCUSSION

Currently, overweight and obesity are the most established associated factors of NAFLD, and are considered, even with some limitation, actual risk factors and putative, indirect causative factors[2-3]. Nonetheless, other and quite neglected factors were and are studied: most of them are related to behaviour, such as physical activity[5], sleep habits[4] and sun exposure, this last with a likely effects on vitamin D status[22]. Nutrition has a qualitative profile, and not only a quantitative one, *i.e.,* not only caloric intake, so that the association of unhealthy dietary habits, apart the abuse of alcohol, is associated with unhealthy liver and, notably, NAFLD. This is confirmed in our study in which we observe that, apart the greater BMI, also a poorer adherence to Mediterranean Diet profile[5], widely and since several years used as a proxy of healthy diet, strongly predicts the occurrence of NAFLD, independently from overweight. Also the almost reciprocal Western Diet profile displays an unfavourable relationship for the occurrence of NAFLD. This is confirmed in our study by the significant difference of averages, with a greater Western Diet score in NAFLD (Table 1), by the greater odds of NAFLD associated with greater BMI and Western Diet habits, and with lower adherence to Mediterranean Diet (Table 2). Moreover, by a model of multivariate analysis (Table 3) the effects of BMI, Mediterranean Diet and Western Diet are independently operating, addressing clearly to the opposite effects of Mediterranean Diet (favourable) and of Western Diet and overweight (detrimental). Concurrently with nutritional profiles and BMI, sedentary life, assessed quantitatively as physical activity score, displays the same effects: a better physical exercise profile is associated with a lower prevalence (Table 2) and severity of bright liver score (Table 3), as assessed in NAFLD by liver ultrasound. Physical activity score is overall poorer in NAFLD *vs* controls (Table 1). The same association is observed for the sun exposure score, which is greater in controls (Table 1) and which may indicate, apart a greater open air life, also a better D vitamin status, important because vitamin D deficiency is associated with NAFLD[22]. Differently from the observation reported in youngsters[4], sleep hours do not show any significant relationship with NAFLD.

We must acknowledge several limitations of our study. First, the overall, comparison between NAFLD patients and controls (Table 1) does not display extreme differences, even if they are statistically significant, when considering sleep hours, sun exposure, adherence to Mediterranean Diet Score and physical activity. There are very different features considering the greater score of Western Diet profile pattern in NAFLD. These even small differences between NAFLD and controls become more relevant within the model that takes into account all the co-variates, so that we must still consider them as relatively important features regarding NAFLD, even envisaging a size effect in the group studied.

Second limitation is that our eligibility criteria were rather strict, resulting in a population without significant co-morbidities, since all patients with diabetes and/or even minimally elevated ALT levels were excluded. It is possible that the analyzed lifestyle measures might work differently in a more comprehensive NAFLD cohort that includes other associated diseases. Scope of the study was to investigate NAFLD as an almost-isolated disease, and even with these restrictions association of recognized and neglected aspects of lifestyle are seemingly operating.

Modification over the time of healthier nutritional and behavioural profiles is a very articulated topic of investigation, which includes also the need of assessing the process of erosion of traditionally cohesive family and community relationships[24] with effects on health and mortality. Such studies have a counterpart in the current societal issue aimed at the preservation of traditional habits, and even clinical conditions, such as high hemoglobin levels[25] which often are credited as healthier. Many animal models have been studied in which dietary variations produce liver injury, and by extrapolation, malnutrition, particularly deficiencies of protein and vitamins has long been considered an important factor in human cirrhosis when no evidence existed for another aetiology; by contrast, weight reduction through low-calorie diets or starvation reduces the steatosis resulting from obesity[1]. Malnutrition was in the last century, and now again, the key of many disease and, notably of liver disease, with its paradigm of fatty liver evolving toward fibrosis. Apart the pioneering studies on lifestyle changes[26] we are still on the starting blocks because each aspect of lifestyle is studied, and thereafter assessed and managed as an individual factor. Despite the great attention which is devoted in Europe to healthier environment and to urban mobility, using the paradigm of Smart City, few or no research are at the moment published and available, even if elsewhere there is already a move in this sense also by comprehensive approach focused to clinical risk assessment and management[2]. The important most recent reviews appropriately address benefits of healthy diet and exercise on NAFLD[27] both in adults[28] and in children[29], even if other factors, genetic[30], behavioural and environmental should not be neglected[31,32]. The opportunity for the medicine are relevant since articulated clinical intervention, which, according to our results, are justified, can be pursued with a focus on nutritional profile, physical exercise mainly open-air for enhancing sun exposure and improving sleep duration and rhythm[33], cultural and traditional medicine issues and, comprehensively, the quality of life[34-39]. The pre-requisite is that both medical doctor and patient should not be mucking around in search of the magic bullet, and instead try to take seriously and with a strategy the road of lasting lifestyle change. Individual, professional and societal benefits are the outcomes that can be reached[2].

**COMMENTS**

***Background***

In a very simplified manner today we tend to describe the lifestyles in medicine especially in terms of diet and physical inactivity or sedentary life, with a synergistic effect on body size – obesity – and on disease related with excessive food intake (atherosclerosis and liver disease).

***Research frontiers***

Many animal models have been studied in which dietary variations produce liver injury, and by extrapolation, malnutrition, particularly deficiencies of protein and vitamins has long been considered an important factor in human cirrhosis when no evidence existed for another aetiology; by contrast, weight reduction through low-calorie diets or starvation reduces the steatosis resulting from obesity.

***Innovations and breakthroughs***

This is confirmed in our study in which we observe that, apart the greater BMI, also a poorer adherence to Mediterranean Diet profile, widely and since several years used as a proxy of healthy diet, strongly predicts the occurrence of NAFLD, independently from overweight. Also the almost reciprocal Western Diet profile displays an unfavourable relationship for the occurrence of NAFLD. This is confirmed in our study by the significant difference of averages, with a greater Western Diet score in NAFLD, by the greater odds of NAFLD associated with greater BMI and Western Diet habits, and with lower adherence to Mediterranean Diet.

***Applications***

The opportunity for the medicine are relevant since articulated clinical intervention, which, according to our results, are justified, can be pursued with a focus on nutritional profile, physical exercise mainly open-air for enhancing sun exposure and improving sleep duration and rhythm, cultural and traditional medicine issues and, comprehensively, the quality of life. The pre-requisite is that both medical doctor and patient should not be mucking around in search of the magic bullet, and instead try to take seriously and with a strategy the road of lasting lifestyle change. Individual, professional and societal benefits are the outcomes that can be reached.

***Peer-review***

The manuscript of “Neglected features of lifestyle: their relevance in non-alcoholic fatty liver disease” is very interesting.

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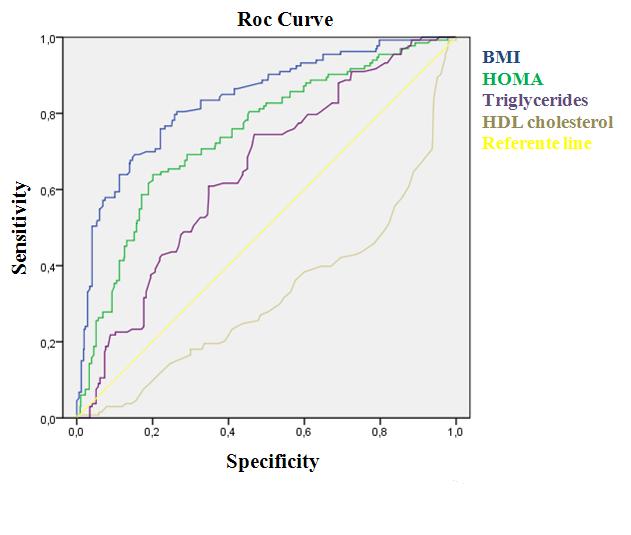
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**Figure 1 Receiver operating characteristic curves of body mass index, homoeostasis model insulin resistance, Triglycerides and high-density lipoprotein -Cholesterol.** The performance of each measure in the prediction of NAFLD is evaluated by the receiver operating characteristic (ROC) curve. The area under the ROC curve (AUROC) and the 95% confidence interval (CI) are used as indexes of accuracy. The optimal cutoff value is determined as the maximum sum of sensitivity and specificity. Accordingly, BMI displays the greater accuracy for predicting NAFLD in comparison of HOMA, Triglycerides and HDL-Cholesterol. The cutoffs are used as thresholds for the calculation of Odds of NAFLD, as reported in Table 2.

**Table 1 Differences between non-alcoholic-fatty-liver-disease and control patients**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **NAFLD**  **(*n* = 532)** | **Controls**  **(*n* = 667)** | ***P* vaule** |
| Age, yr | 48.11 ± 9.00 | 48.60 ± 8.70 | 0.343 |
| Systolic blood pressure (mmHg) | 124.53 ± 9.71 | 121.21 ± 10.80 | < 0.0001 |
| Diastolic blood pressure (mmHg) | 78.84 ± 6.72 | 76.50 ± 6.73 | < 0.0001 |
| BMI, kg/m2 | 30.49 ± 5.55 | 24.44 ± 3.72 | < 0.0001 |
| HOMA | 2.89 ± 1.76 | 1.80 ± 1.28 | < 0.0001 |
| eGFR | 82.49 ± 14.15 | 82.15 ± 17.44 | 0.714 |
| Total cholesterol, mg/dL | 205.17 ± 37.16 | 207.09 ± 38.82 | 0.387 |
| HDL cholesterol, mg/dL | 51.67 ± 15.85 | 61.45 ± 16.41 | < 0.0001 |
| Triglycerides, mg/dL | 109.08 ± 42.41 | 95.23 ± 58.59 | < 0.0001 |
| LDL cholesterol, mg/dL | 131.98 ± 33.45 | 126.59 ± 37.29 | 0.009 |
| γ-GT (U/L) | 33.24 ± 29.40 | 26.03 ± 21.95 | < 0.0001 |
| AST (U/L) | 20.77 ± 5.91 | 21.01 ± 7.10 | 0.530 |
| ALT (U/L) | 15.65 ± 4.60 | 10.40 ± 4.88 | < 0.0001 |
| Alkaline phosphatase (U/L) | 68.37 ± 18.49 | 72.75 ± 43.42 | 0.030 |
| Serum albumin (g/dL) | 4.62 ± 0.39 | 4.53 ± 0.40 | < 0.0001 |
| Lifestyle items | | | |
| AMDS | 32.21 ± 0.91 | 34.91 ± 0.61 | < 0.0001 |
| Baecke - physical activity total score | 39.82 ± 3.60 | 41.43 ± 3.32 | < 0.0001 |
| WDS - Western Diet Score | 22.84 ± 7.87 | 12.73 ± 2.48 | < 0.0001 |
| Sun Exposure Score | 31.43 ± 3.89 | 35.73± 5.25 | < 0.0001 |
| Sleep hours | 7.86 ± 1.31 | 7.90 ± 1.23 | 0.552 |

BMI: Body mass index; HOMA-IR: Homoeostasis model insulin resistance; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; γ –GT: γ-glutamyl transpeptidase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; γ–GT: γ-glutamyl transpeptidase; AMDS: Adherence Mediterranean Diet Score.

**Table 2 Pearson’s χ2 and odds ratio**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **NAFLD** | **Controls** | ***χ2*** | ***P* value** | **OR** | **95%CI** |
| BMI ≥ 26.40 | 408 | 167 | 316.3851 | < 0.0001 | 9.851 | 7.546-12.861 |
| BMI < 26.40 | 124 | 500 |
| HOMA ≥ 1.87 | 368 | 211 | 167.0111 | < 0.0001 | 4.849 | 3.792-6.202 |
| HOMA < 1.87 | 164 | 456 |
| HDL ≥ 54.50 | 204 | 400 | 55.3581 | < 0.0001 | .415 | 0.329-0.524 |
| HDL < 54.50 | 328 | 267 |
| TGL ≥ 94 | 324 | 240 | 73.7751 | < 0.0001 | 2.771 | 2.191-3.506 |
| TGL < 94 | 208 | 427 |
| AMDS ≥ 34 | 32 | 650 | 1008.8311 | < 0.0001 | .002 | 0.001-0.003 |
| AMDS < 34 | 500 | 17 |
| BAECKE ≥ 41.5 | 181 | 354 | 43.4681 | < 0.0001 | .456 | 0.360-0.577 |
| BAECKE < 41.5 | 351 | 313 |
| WDS ≥ 15.5 | 399 | 97 | 445.9811 | < 0.0001 | 17.629 | 13.174-23.590 |
| WDS < 15.5 | 133 | 570 |
| SES ≥ 34.5 | 111 | 348 | 122.7881 | < 0.0001 | .242 | 0.187-0.313 |
| SES < 34.5 | 421 | 319 |
| Sleep hours ≥ 8 | 319 | 370 | 2.5921 | 0.107 | 1.210 | 0.959-1.527 |
| Sleep hours < 8 | *208* | *292* |

1Indicates the thresholds calculated by ROC analysis used as cut-offs for comparison between groups with lower measures (BMI, HOMA, AMDS, WDS, SES, BAECKE) *vs* groups with greater measures. BMI: body mass index; HOMA-IR: homoeostasis model insulin resistance; HDL: high-density lipoprotein; TGL: Triglycerides; AMDS: Adherence to Mediterranean Diet Score; WDS: Western Diet Score; SES: Sun Exposure Score; BAECKE: Baecke’s physical activity questionnaire total score).

**Table 3 Multiple linear regression of variables**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| ***Predictors*** | ***R*** | ***R2*** | ***F*** | ***Sig.*** | ***β*** | ***P* value** |
|  | **0.965** | **0.932** | **2309.100** | **< 0.0001** |  |  |
| BMI, Kg/m2 |  |  |  |  | -0.448 | < 0.0001 |
| HOMA |  |  |  |  | -0.393 | < 0.0001 |
| AMDS |  |  |  |  | -1.398 | < 0.0001 |
| Baecke |  |  |  |  | -0.074 | < 0.0001 |
| WDS |  |  |  |  | 0.069 | < 0.0001 |
| Sun Exposure Score |  |  |  |  | -0.044 | < 0.0001 |
| Sleep hours |  |  |  |  | -0.008 | 0.296 |

Weighted Least Squares Regression – Weighted by Age. BMI: body mass index; HOMA-IR: homoeostasis model insulin resistance; AMDS: Adherence to Mediterranean Diet Score; WDS: Western Diet Score; SES: Sun Exposure Score; BAECKE: Baecke’s physical activity questionnaire total score) and sleep hours *vs* the severity of NAFLD, assessed by ultrasound as BLS (bright liver score); NAFLD: Included in this analysis as a categorical variable with all 3 severity grades.