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Relationship between the Finnish Diabetes Risk Score (FINDRISC), vitamin D levels, and insulin resistance in obese subjects

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ABSTRACT

Aim: To assess the relationship between 25-hydroxyvitamin D [25(OH)D] blood concentrations in subjects with obesity and type 2 diabetes mellitus (T2D) risk according to the Finnish Diabetes Risk Score (FINDRISC) modified for Latin America (LA-FINDRISC).
Methods: This study was conducted in Ciudad Bolívar, Venezuela. Eighty two women and 20 men (53 obese and 49 nonobese), with an average age of 42.6 ± 12.30 years were enrolled. Weight, height, body mass index (BMI), waist circumference (WC), fasting glucose, basal insulin, plasma lipids, Homeostasis Model Assessment-Insulin Resistance (HOMA-IR), and 25(OH)D levels were measured. FINDRISC with WC cutoff points modified for Latin America was applied.
Results: No difference in 25(OH)D levels between obese and nonobese subjects was found. When anthropometric, clinical, and biochemical variables according to the 25(OH)D status were compared, the only difference detected was higher LA-FINDRISC in the insufficient/low 25(OH)D group compared to normal 25(OH)D levels group (12.75 ± 6.62; vs 10.15 ± 5.21; $p = 0.031$). LA-FINDRISC was negatively correlated with plasma 25(OH)D levels ($r = -0.302$; $p = 0.002$) and positively correlated with the HOMA-IR index ($r = 0.637$; $p = 0.0001$).
Conclusions: The LA-FINDRISC significantly correlated with both 25(OH)D levels and insulin resistance markers in this group of patients.

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1. Introduction

Vitamin D (VD) is considered a complex steroid-hormonal system that regulates calcium homeostasis, and participates in autocrine, paracrine, and endocrine processes [1,2]. 25-Hydroxyvitamin D [25(OH)D] deficiency is highly prevalent worldwide, especially in the elderly [3], post-menopausal women [4], pregnant women [5], and adolescent girls [6]. It has also been associated with obesity [7]. A meta-analysis showed a 4% reduction in 25(OH)D for every 10% increase of body mass index (BMI) [7]. An inverse relationship between 25(OH)D and adipocyte size has been reported [8]. Interestingly, VD could protect again diet-induced obesity by enhancing fatty acid oxidation [9]. Similarly, 25(OH)D deficiency has been associated with β-cell dysfunction and insulin resistance [10]. In fact, it has been shown that VD supplementation may improve the ability of the cells of the islets to synthesize many proteins de novo and to convert proinsulin to insulin [11].

The Finnish Diabetes Risk Score (FINDRISC) is the most widely tool used to identify subjects with high risk of developing type 2 diabetes mellitus (T2D) [12]. A modified version for Latin America [13] (LA-FINDRISC), using different waist circumference (WC) cutoff values, has been validated [14]. To the best of our knowledge, no previous studies have reported the association between 25(OH)D levels and FINDRISC in subjects with and without obesity. This association is important for understanding the etiology of abnormal glucose metabolism; and from a public health standpoint, it may indicate a need for VD supplementation in patients at high risk according to LA-FINDRISC. Thus, the objective of the present study was to assess the relationship between 25(OH)D blood concentrations and T2D risk according to the LA-FINDRISC.

2. Material and methods

2.1. Design and subjects

An observational, cross-sectional study was designed. Subjects were invited through local newspapers and social media to participate in a screening for cardiometabolic risk. The study comprised 102 subjects; 49 (48.1%) obese (BMI $\geq 30\,kg/m^2$) and 53 (51.9%) nonobese individuals of both sexes, 18 and older. Subjects with a history of coronary heart disease, stroke, chronic kidney disease, osteopenia, and/or osteoporosis, primary hyperlipidemia, diabetes, thyroid or parathyroid diseases, Cushing's syndrome, acromegaly, or any other metabolic disease were excluded, as well those using medication containing calcium or VD.

The data for the study, which was conducted in Ciudad Bolívar, Venezuela, were collected between January–August, 2015. The study was approved by the hospital's Ethics Commission pursuant to Helsinki Declaration guidelines.

2.2. Clinical evaluation

Weight and height were measured with subjects wearing only their underwear. BMI was calculated as weight in kilograms divided by height in meters squared. WC was measured midway between the underside of the lowest rib and the iliac crest, in centimeters, with subjects standing. Blood pressure, expressed in mmHg, was taken on the right arm, with the subject in a sitting position after 10 min of rest, using the auscultation method with a conventional mercury sphygmomanometer.

2.3. Biochemical variables

After obtaining a blood sample from the antecubital vein of subjects fasting for at least eight hours, blood glucose and lipids [total cholesterol, triglycerides and high density lipoprotein cholesterol (HDL-C)] were measured in mg/dL by enzymatic methods. Low density lipoprotein cholesterol (LDL-C) was calculated by means of the Friedewald equation: LDL-C (mg/dL) = total cholesterol − [HDL-C + (triglycerides/5)]. Basal insulin was measured in mU/mL and determined by chemiluminescence with Siemens reagents. Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) was calculated using the equation [fasting glucose (mg/dL) × fasting insulin (mU/mL)/405]. Serum 25(OH)D was determined by Enzyme-Linked ImmunoSorbent Assay (ELISA) with reagents supplied by IBL International GmbH, and was measured in ng/mL. The inter-assay coefficient of variation was 4.6–8.7%; and the intra-assay, 5.3–6.7%. According to the American Society of Endocrinology, 25(OH)D levels between 30–100 ng/mL were considered normal or "sufficient"; levels between 21–29 ng/mL, "insufficient"; and those rating at 20 ng/mL or less were deemed "low" [15].

2.4. LA-FINDRISC

The LA-FINDRISC questionnaire comprises eight variables: age, BMI, WC, physical activity, daily consumption of vegetables and fruits, antihypertensive drug use, personal history of hyperglycemia, and family history of diabetes. WC cutoff values were adjusted for Latin America [13] by adding four points to subjects with abdominal obesity (WC ≥94 cm in men and ≥90 cm in women) and no points to those with WC normal values [14], total score ranging from 0 to 26 points. Subjects scoring ≤14 points were considered at "low-moderate risk," and those with >14 points, at "high risk". These cutoff values have been reported to detect the presence of impaired glucose regulation (prediabetes + unknown T2D) in clinical Venezuelan settings [14].

2.5. Statistical analysis

Continuous variables were presented as mean ± standard deviation; and categorical variables, as absolute number and percentage. Differences between male and female participants were determined through a chi square test. A t-test was performed to assess differences between normally distributed continuous variables, and a Mann–Whitney U test for non-normally distributed variables (systolic and diastolic blood pressure). A Pearson correlation matrix measured the association between the variables. In addition, a multivariate logistic regression analysis using high or low T2D risk according to FINDRISC as a dependent variable was done. All those variables showing statistical significance in the uni-

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Table 1 – Anthropometric, clinical and biochemical variables.

Characteristics	All n = 102	No obese n = 53	Obese n = 49
Female/male	82 (80.4%)/20 (19.6%)	44 (83.0%)/9(17.0%)	38(77.6%)/11(22.4%)
Age (years)	42.56 ± 12.30	42.26 ± 13.65	42.89 ± 10.80
BMI[a] (kg/m^2)	30.60 ± 7.06	25.40 ± 2.80	36.23 ± 5.85***
WC[b] (cm)	93.94 ± 17.69	82.53 ± 11.49	106.27 ± 14.72***
SBP[c] (mmHg)	122.84 ± 14.76	116.60 ± 11.67	129.59 ± 14.88***
DBP[d] (mmHg)	75.63 ± 8.66	72.92 ± 7.87	78.57 ± 8.59 **
Fasting blood glucose (mg/dL)	94.29 ± 11.64	94.18 ± 12.02	94.40 ± 11.35
Basal insulin (mU/mL)	16.27 ± 7.86	12.03 ± 6.34	20.85 ± 6.71***
HOMA-IR[e]	3.81 ± 1.93	2.81 ± 1.51	4.88 ± 1.76***
Total cholesterol (mg/dL)	174.02 ± 36.93	167.08 ± 35.27	181.53 ± 37.56 *
LDL-C[f] (mg/dL)	105.48 ± 32.70	97.60 ± 29.65	114.00 ± 33.98 *
HDL-C[g] (mg/dL)	46.08 ± 12.31	49.58 ± 12.56	42.30 ± 10.95**
Triglycerides (mg/dL)	112,29 ± 52.65	99.47 ± 47.01	126.15 ± 55.32*
25(OH)D[h] (ng/mL)	38.60 ± 17.89	39.17 ± 18.25	37.97 ± 17.66
LA-FINDRISC[i]	11.09 ± 5.87	7.71 ± 5.00	14.75 ± 4.37***

Data are present as X ± SD. Categorical are N (%).
[a] BMI: body mass index.
[b] WC: waist circumference.
[c] SBP: systolic blood pressure.
[d] DBP: diastolic blood pressure.
[e] HOMA-IR: Homeostasis Model Assessment-Insulin Resistance.
[f] LDL-C: low density lipoprotein cholesterol.
[g] HDL-C: high density lipoprotein cholesterol.
[h] 25(OH)D: 25-hydroxyvitamin D.
[i] LA-FINDRISC: Latin American Finnish Diabetes Risk Score.
* $p < 0.05$.
** $p < 0.002$.
*** $p < 0.001$.

variate analysis were included as independent variables. All calculations were performed using SPSS Statistics 20.0 program (IBM Corp. Released 2011. Armonk, NY: USA), a p-value of <0.05 being statistically significant.

3. Results

Obese subjects revealed higher values of BMI, WC, blood pressure, basal insulin, HOMA-IR, lipid values (lower HDL-C), and LA-FINDRISC than non-obese subjects ($p < 0.05$), both groups having similar 25(OH)D (Table 1).

When subjects were categorized according to 25(OH)D levels, only LA-FINDRISC showed higher values in subjects with insufficient or low 25(OH)D, compared to those with normal 25(OH)D levels ($p = 0.031$).

When subjects were categorized according to the LA-FINDRISC, those at high risk (>14 points) had higher values for both the components that add points to the score (age, BMI, and WC) and other cardiometabolic risk factors (blood pressure, blood glucose, basal insulin and HOMA-IR); as well as lower HDL-C and 25(OH)D values than those with low-moderate risk of T2D ($p < 0.01$) (Table 2).

In the Pearson correlation analysis the LA-FINDRISC showed a significantly negative correlation with 25(OH)D concentration ($r = -0.302$; $p = 0.002$) and HDL-C ($r = -0.292$; $p = 0.003$); and a significantly positive correlation with HOMA-IR ($r = 0.637$; $p < 0.0001$) and basal insulin ($r = 0.563$; $p < 0.0001$) (Fig. 1).

A large proportion of subjects with low-insufficient 25(OH)D levels were found in the group at high risk of T2D (LA-FINDRISC > 14 points), relative to those with low-moderate (≤14 points) risk of T2D (51.5% vs 29.0%, respectively; $p = 0.027$) (Fig. 2). The risk of having low-insufficient 25(OH)D levels was 160% (OR 2.6; CI 95% 1.10–6.14) higher in subjects with more than 14 points in the LA-FINDRISC than those with 14 or fewer points. Additionally, subjects with a LA-FINDRISC >14 points have higher levels of insulin resistance measured by HOMA-IR than those with ≤ 14 points (93.9% vs 56.5%; $p = 0.0001$) (Fig. 3). The risk of insulin resistance in this group (>14 points) was 11 times higher than those with ≤14 points (OR: 11.92; CI 95%: 2.64–53.81).

A logistic regression analysis was performed using high or low T2D risk according to FINDRISC as a dependent variable, and including as independent variables those having had statistical significance in the univariate analysis; to wit, age ($p = 0.03$); BMI ($p = 0.0001$); systolic blood pressure ($p = 0.0001$); diastolic blood pressure ($p = 0.003$); HOMA-IR ($p = 0.0001$); and 25(OH)D ($p = 0.01$). The multivariate analysis revealed that BMI, systolic and diastolic blood pressure lost their statistical significance, age (odds ratio: 1.07; CI 95%: 1.01–1.12; $p = 0.009$), and HOMA-IR (odds ratio: 2.44; CI 95%: 1.64–3.64; $p = 0.0001$) remaining as independent T2D risk factors; and 25(OH)D (odds ratio: 0.93; CI 95%: 0.89–0.98; $p = 0.005$) as independent protective factor with a square R of 0.534.

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Table 2 – Subjects characteristics categorized to type 2 diabetes risks according to LA-FINDRISC.

Characteristics	Low-moderate risk (≤14 points) n = 69	High risk (>14 points) n = 33
Age (years)	39.93 ± 12.23	48.09 ± 10.66**
BMI[a] (kg/m^2)	28.71 ± 6.31	34.56 ± 6.99***
WC[b] (cm)	89.33 ± 16.89	103.56 ± 15.52***
SBP[c] (mmHg)	119.06 ± 12.87	130.75 ± 15.51***
DBP[d] (mmHg)	73.77 ± 8.46	79.54 ± 7.84**
Fasting blood glucose (mg/dL)	90.59 ± 9.95	102.03 ± 11.25***
Basal insulin (mU/mL)	13.97 ± 7.46	21.07 ± 6.45***
HOMA-IR[e]	3.11 ± 1.68	5.27 ± 1.61***
Total cholesterol (mg/dL)	173.84 ± 36.93	174.41 ± 37.51
LDL-C[f] (mg/dL)	104.22 ± 31.93	108.12 ± 34.63
HDL-C[g] (mg/dL)	47.65 ± 13.19	42.80 ± 9.63*
Triglycerides (mg/dL)	109.85 ± 54.14	117.40 ± 49.83
25(OH)D[h] (ng/mL)	41.57 ± 18.83	32.38 ± 14.07*

Variables are X ± SD.
[a] BMI: body mass index.
[b] WC: waist circumference.
[c] SBP: systolic blood pressure.
[d] DBP: diastolic blood pressure.
[e] HOMA-IR: Homeostasis Model Assessment-Insulin Resistance.
[f] LDL-C: low density lipoprotein cholesterol.
[g] HDL-C: high density lipoprotein cholesterol.
[h] 25(OH)D: 25-hydroxyvitamin D.
* $p < 0.01$.
** $p < 0.001$.
*** $p < 0.0001$.

4. Discussion

In this group of Latin Americans from Venezuela, LA-FINDRISC was associated with 25(OH)D plasma concentrations. Subjects with an increased risk of T2D as assessed by LA-FINDRISC had lower 25(OH)D concentration and a greater degree of insulin resistance (HOMA-IR). 25(OH)D concentrations did not differ between subjects with or without obesity.

The FINDRISC is the most widely used screening tool for undiagnosed T2D. It includes anthropometric (BMI and WC), metabolic, and lifestyle factors that predict T2D and alterations in glucose metabolism [10,14]. An external validation of the original FINDRISC (LA-FINDRISC) including the Latin America abdominal obesity cutoffs (≥94 cm for men and ≥90 cm for women) [13] has been developed [14]. As expected, and consistent with previous reports [17,18], subjects with high risk for T2D (LA-FINDRISC > 14 points) had higher age, BMI, WC, blood pressure, blood glucose, basal insulin, HOMA-IR and lower HDL-C than those with low-moderate risk for T2D (LA-FINDRISC ≤ 14 points). Janghorbani et al. [17] reported that subjects at high risk according to FINDRISC had 4.8 more chances to develop metabolic syndrome (MS) than those at low risk, FINDRISC emerging not only as a T2D detecting tool but also as one to identify subjects with elevated global cardiometabolic risk. In our study, as in previous ones [18,19], HDL-C showed a negative correlation with the FINDRISC scale, which might be explained by the inverse relation that the FINDRISC components have with HDL-C [20–22].

The main contribution of this study was finding that a high diabetes risk according to LA-FINDRISC (>14 points) is associated with a higher risk of low/insufficient 25(OH)D levels. This higher risk of T2D increased 2.6 times the chance of having a low-insufficient 25(OH)D concentration compared with low-moderate T2D risk. Besides, a significantly negative correlation was found between plasma 25(OH)D concentration and the LA-FINDRISC scale.

This is the first report relating the association between the LA-FINDRISC and 25(OH)D concentration. However, other epidemiologic studies have prospectively evaluated the association between 25(OH)D levels and T2D risk. One of them, including 4097 healthy subjects from Finland with a 17-year follow-up, evidenced an inverse correlation between 25(OH)D levels and T2D risk [23]. Likewise, Forouhi et al. [24], in a cohort study in the English population of Ely, demonstrated that 25(OH)D levels correlated negatively with T2D risk at 10 years of follow-up. These results are consistent with those in this report, as the FINDRISC has widely demonstrated the capability of predicting T2D risk by up to 10 years [12,16].

Some mechanisms might explain the relation between 25(OH)D levels and T2D risk. Beta pancreatic cells express the VD receptor, promoting calcium absorption and its subsequent utilization for insulin secretion. In addition, allelic variations in the genes involved in VD metabolism and in the synthesis of its receptor are associated with impaired glucose tolerance, decreased insulin secretion and sensitivity, and increased inflammation [25]. A growing body of evidence indicates that hypovitaminosis D is associated with higher serum levels of inflammatory biomarkers [26,27]. The relationship between 25(OH)D levels and low-intensity chronic inflammation with insulin resistance can be mediated in part by the immune-modulating properties of VD, which is able to downregulate the production of pro-inflammatory cytokines [1,26].

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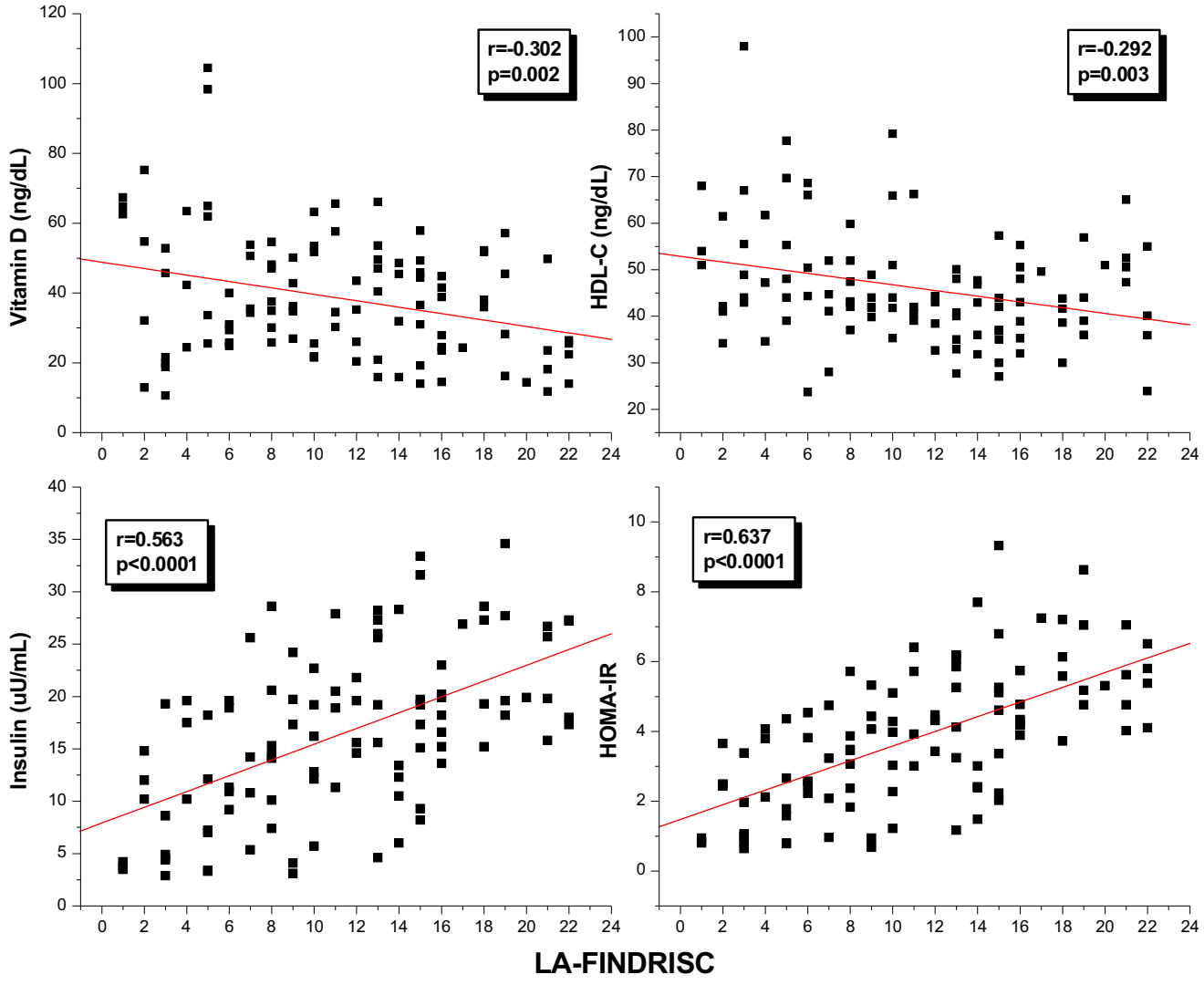

Fig. 1 – Correlation between T2D risk according to LA-FINDRISC and plasma concentration of vitamin D, high density lipoprotein cholesterol (HDL-C), basal insulin, and insulin resistance index (HOMA-IR).

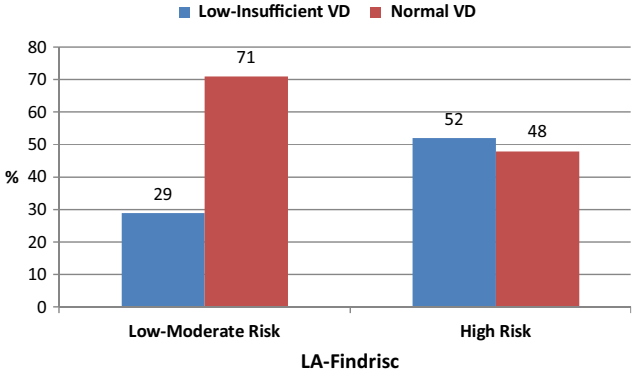

Fig. 2 – Association between T2D risk according to LA-FINDRISC (low-moderate or high) and vitamin D concentration (VD-low-insufficient or normal). Chi square p = 0.027; odds ratio 2.6 (CI 95%: 1.10–6.14).

The negative correlation between the LA-FINDRISC, basal insulin, and HOMA-IR – a surrogate marker of insulin resistance widely used in different populations [28] – is in agreement with that of other reports [29,30]. Moreover, subjects with high risk to develop T2D presented a higher rate (OR 11.92) of insulin resistance than subjects with lower to moderate T2D risk.

Previous reports have documented that FINDRISC is more strongly related to insulin resistance than to impaired insulin secretion [30], as confirmed in a study including 7232 Finnish men [31]. Since most of the times insulin resistance precedes T2D diagnosis, the FINDRISC might be useful in identifying the disease at an early stage. Moreover, it has been shown that FINDRISC's ability to detect insulin resistance is even greater than its ability to identify previously undiagnosed T2D, thus increasing its clinical relevance [32].

Other reports have shown that obesity is associated with low 25(OH)D concentrations [7,33]; however, no difference in

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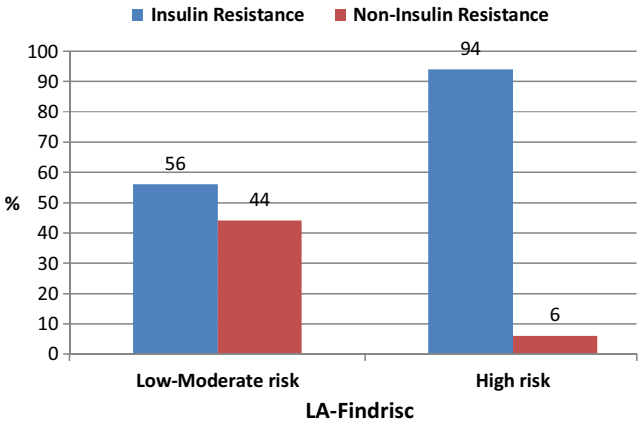

Fig. 3 – Association between T2D risk according LA-FINDRISC and insulin resistance by HOMA-IR. Chi square: p = 0.0001; odds ratio: 11.92 (CI 95%: 2.64–53.81).

25(OH)D levels was observed in this report with regards to obesity. Perhaps, the small sample size can reduce the probable difference. Besides, factors such as physical activity, smoking, UV exposure, and use of sunscreen lotions, which we are unaware of in the subjects evaluated, might have a bearing on serum concentrations of 25(OH)D. Intense physical activity has been shown to correlate with an increase in 25(OH)D serum concentrations independently of BMI [34]. Contrarily, smoking is associated with low levels of 25(OH)D possibly due to the inhibiting effects of metabolic derivatives of naphthalene (a cigarette metabolite) such as tetralone, on CYP27A1 [35]. Additionally, any barrier to UV radiation into the skin epidermis and dermis is inversely correlated with circulating 25(OH)D levels [2,6]. This includes the use of sunblockers which might significantly hinder VD production [2].

Similarly, no differences were observed between age, BMI, WC, blood pressure, fasting blood glucose, basal insulin, HOMA-IR, and lipid values according to 25(OH)D concentrations. This finding is consistent with that reported by Reis et al. [36] in a Southern California Community, and with another by Rueda et al. [37] in severely obese subjects, in which no relationship between MS components and 25(OH)D concentration was found. Contrarily, in a larger sample (834 men and 820 women) from the 2003–2004 US National Health and Nutrition Examination Survey (NHANES), Reis et al. [38] found, after adjusting for many confounding variables, an inverse association between 25(OH)D levels and MS. Different levels of UV exposure explain this difference: those residing in sunny and all-year-round temperate Southern California [36] almost duplicated VD concentration relative to the populations in the NHANES study [38], suggesting that higher 25(OH)D levels may not be related to MS. Miñambres et al. [39] also reported a significant association between MS components and 25(OH)D levels independently of the presence of obesity. Probably, part of the difference observed was based on both the characteristics of the subjects evaluated and the methodology to assess 25(OH)D concentrations.

4.1. *Study limitations*

Some limitations can be found in the present study. First, the classification of high risk used (>14 points) derives from studies of European populations. However, the risk factors included are globally prevalent, and an adapted WC cutoff value was applied [13] to improve the FINDRISC sensitivity in Latin American subjects. An external validation in Venezuelan subjects found that more than 14 points of LA-FINDRISC improve the detection of subjects with impaired glucose regulation, especially in women [14], who represent 80% of the sample in the study. Second, the FINDRISC was created for detection of T2D risk or impaired glucose metabolism, not for 25(OH)D deficit. Third, this is a cross sectional study, therefore it is not possible to ensure that subjects with low 25(OH)D levels will have an increase in T2D incidence. Nonetheless, other studies of similar design have demonstrated the association between FINDRISC and other cardiometabolic markers [18,40]. Finally, the subjects in this study were recruited from cardiometabolic risk screening sessions, and might not represent the general population.

5. Conclusion

In this study, LA-FINDRISC significantly correlated with both 25(OH)D levels and insulin resistance markers. 25(OH)D levels alone may not be sufficient to determine T2D risk. Based on the results found in this study, it might be recommendable that plasma concentration of 25(OH)D be assessed in all those subjects in Ciudad Bolivar presenting a LA-FINDRISC score ≥14. Further research is necessary to explain why obesity did not affect 25(OH)D levels in this population.

Conflict of interest

The authors state that they have no conflict of interest.

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REFERENCES

[1] M.F. Holick, Vitamin D deficiency, N. Engl. J. Med. 357 (2007) 266–281.
[2] P. Lips, Vitamin D physiology, Prog. Biophys. Mol. Biol. 92 (2006) 4–8.
[3] M.F. Holick, High prevalence of vitamin D inadequacy and implications for health, Mayo Clin. Proc. 81 (2006) 353–373.
[4] M.F. Holick, E.S. Siris, N. Binkley, et al., Prevalence of vitamin D inadequacy among postmenopausal North American

women receiving osteoporosis therapy, J. Clin. Endocrinol. Metab. 90 (2005) 3215–3224.
[5] P.M. Brannon, M.F. Picciano, Vitamin D in pregnancy and lactation in humans, Annu. Rev. Nutr. 31 (2011) 89–115.
[6] T.R. Hill, A.A. Cotter, S. Mitchell, et al., Vitamin D status and its determinants in adolescents from the Northern Ireland Young Hearts 2000 cohort, Br. J. Nutr. 99 (2008) 1061–1067.
[7] P. Saneei, A. Salehi-Abargouei, A. Esmaillzadeh, Serum 25-hydroxy vitamin D levels in relation to body mass index: a systematic review and meta-analysis, Obes. Rev. 14 (2013) 393–404.
[8] M. Caron-Jobin, A.S. Morisset, A. Tremblay, et al., Elevated serum 25(OH)D concentrations, vitamin D, and calcium intakes are associated with reduced adipocyte size in women, Obesity (Silver Spring) 19 (2011) 1335–1341.
[9] J. Marcotorchino, F. Tourniaire, J. Astier, et al., Vitamin D protects again diet-induced obesity by enhancing fatty acid oxidation, J. Nutr. Biochem. 25 (2014) 1077–1083.
[10] K.C. Chiu, A. Chu, V.L. Go, M.F. Saad, Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction, Am. J. Clin. Nutr. 79 (2004) 820–825.
[11] J. Wranicz, D. Szostak-Wegierek, Health outcomes of vitamin D. Part II. Role in prevention of diseases, Rocz. Panstw. Zakl. Hig. 65 (2014) 273–279.
[12] J. Lindstrom, J. Tuomilehto, The diabetes risk score: a practical tool to predict type 2 diabetes risk, Diabetes Care 26 (2003) 725–731.
[13] P. Aschner, R. Buendía, I. Brajkovich, et al., Determination of the cutoff point for waist circumference that establishes the presence of abdominal obesity in Latin American men and women, Diabetes Res. Clin. Pract. 93 (2011) 243–247.
[14] P. Aschner, R. Nieto-Martínez, A. Marin, M. Ríos, Validation of the FINDRISC score as a screening tool for people with impaired glucose regulation in Latin America using modified regional cut-off points for waist circumference, Minerva Endocrinol. 37 (2012) 114.
[15] M. Holick, N. Binkley, H. Bischoff-Ferrari, et al., Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline, J. Clin. Endocrinol. Metab. 96 (2011) 1911–1930.
[16] P.E. Schwarz, J. Li, J. Lindstrom, J. Tuomilehto, Tools for predicting the risk of type 2 diabetes in daily practice, Horm. Metab. Res. 41 (2009) 86–97.
[17] M. Janghorbani, H. Adineh, M. Amini, Evaluation of the Finnish Diabetes Risk Score (FINDRISC) as a screening tool for the metabolic syndrome, Rev. Diabet. Stud. 10 (2013) 283–292.
[18] P. Djurić, Z. Mladenović, A. Grdinić, et al., Correlation between the Finnish Diabetes Risk Score and the severity of coronary artery disease, Vojnosanit. Pregl. 71 (2014) 474–480.
[19] K. Makrilakis, S. Liatis, S. Grammatikou, et al., Validation of the Finnish diabetes risk score (FINDRISC) questionnaire for screening for undiagnosed type 2 diabetes, dysglycaemia and the metabolic syndrome in Greece, Diabetes Metab. 37 (2011) 144–151.
[20] H. Florez, E. Silva, V. Fernández, et al., Prevalence and risk factors associated with the metabolic syndrome and dyslipidemia in White, Black Amerindian and Mixed Hispanics in Zulia, State, Venezuela, Diabetes Res. Clin. Pract. 69 (2005) 63–77.
[21] P.J. Barter, The causes and consequences of low levels of high density lipoproteins in patients with diabetes, Diabetes Metab. J. 35 (2011) 101–106.
[22] S. Song, E.K. Kim, S. Hong, et al., Low consumption of fruits and dairy foods is associated with metabolic syndrome in Korean adults from outpatient clinics in and near Seoul, Nutr. Res. Pract. 9 (2015) 554–562.
[23] C. Mattila, P. Knekt, S. Männistö, et al., Serum 25-hydroxyvitamin D concentration and subsequent risk of type 2 diabetes, Diabetes Care 30 (2007) 2569–2570.
[24] N.G. Forouhi, J. Luan, A. Cooper, et al., Baseline serum 25-hydroxy vitamin D is predictive of future glycemic status and insulin resistance: the Medical Research Council Ely Prospective Study 1990-2000, Diabetes 57 (2008) 2619–2625.
[25] T. Takiishi, C. Gysemans, R. Bouillon, C. Mathieu, Vitamin D and diabetes, Rheum. Dis. Clin. North Am. 38 (2012) 179–206.
[26] B. Thorand, A. Zierer, C. Huth, et al., Effect of serum 25-hydroxyvitamin D on risk for type 2 diabetes may be partially mediated by subclinical inflammation: results from the MONICA/KORA Augsburg study, Diabetes Care 34 (2011) 2320–2322.
[27] C. Ding, V. Parameswaran, L. Blizzard, et al., Not a simple fat-soluble vitamin: changes in serum 25-(OH)D levels are predicted by adiposity and adipocytokines in older adults, J. Int. Med. 268 (2010) 501–510.
[28] D.R. Matthews, J.P. Hosker, A.S. Rudenski, et al., Homeostasis model assessment: insulin resistance and β-cell function from fasting plasma glucose and insulin concentrations in man, Diabetologia 28 (1985) 412–419.
[29] P.E. Schwarz, J. Li, M. Reimann, et al., The Finnish Diabetes Risk Score is associated with insulin resistance and progression towards type 2 diabetes, J. Clin. Endocrinol. Metab. 94 (2009) 920–926.
[30] K.G. Brodovicz, J.M. Dekker, J.M. Rijkelijkhuizen, et al., The Finnish Diabetes Risk Score is associated with insulin resistance but not reduced β-cell function, by classical and model-based estimates, Diabet. Med. 28 (2011) 1078–1081.
[31] J. Wang, A. Stancáková, J. Kuusisto, M. Laakso, Identification of undiagnosed type 2 diabetic individuals by the finnish diabetes risk score and biochemical and genetic markers: a population-based study of 7232 Finnish men, J. Clin. Endocrinol. Metab. 95 (2010) 3858–3862.
[32] A. Bergmann, J. Li, L. Wang, et al., A simplified Finnish diabetes risk score to predict type 2 diabetes risk and disease evolution in a German population, Horm. Metab. Res. 39 (2007) 677–682.
[33] S. Vanlint, Vitamin D and obesity, Nutrients 5 (2013) 949–956.
[34] D. Scott, L. Blizzard, J. Fell, et al., A prospective study of the associations between 25-hydroxyvitamin D, sarcopenia progression, and physical activity in older adults, Clin. Endocrinol. (Oxf.) 73 (2010) 581–587.
[35] A.S. Aboraia, B. Makowski, A. Bahja, et al., Synthesis and CYP24A1 inhibitory activity of (*E*)-2-(2-substituted benzylidene)- and 2-(2-substituted benzyl)-6-methoxy-tetralones, Eur. J. Med. Chem. 45 (2010) 4427–4434.
[36] J.P. Reis, D. von Mühlen, D. Kritz-Silverstein, et al., Vitamin D, parathyroid hormone levels, and the prevalence of metabolic syndrome in community-dwelling older adults, Diabetes Care 30 (2007) 1549–1555.
[37] S. Rueda, C. Fernández-Fernández, F. Romero, et al., Vitamin D, PTH, and the metabolic syndrome in severely obese subjects, Obes. Surg. 18 (2008) 151–154.
[38] J.P. Reis, D. von Mühlen, E.R. Miller 3rd, Relation of 25-hydroxyvitamin D and parathyroid hormone levels with metabolic syndrome among US adults, Eur. J. Endocrinol. 159 (2008) 41–48.
[39] I. Miñambres, J. Sánchez-Hernández, J.L. Sánchez-Quesada, et al., The association of hypovitaminosis D with the metabolic syndrome is independent of the degree of obesity, ISRN Endocrinol. 2012 (2012) 691803.
[40] J.A. Carvalho, N.C. Barengo, J. Tuomilehto, et al., The Finnish Diabetes Risk Score (FINDRISC) as a screening tool for hepatic steatosis, Ann. Med. 43 (2011) 487–494.

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