Preventive Medicine Reports 24 (2021) 101587

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

Association between deficient and insufficient 25(OH)D serum concentrations and cardiometabolic risk factors: Findings of a population-based study with older adults of southern Brazil

Francieli Cembranel [a,*], Alexandra Crispim Boing [b], Antonio Fernando Boing [b], André Junqueira Xavier [c], Eleonora d'Orsi [b,d]

[a] Public Health Postgraduate Program and Department of Nutrition, Federal University of Santa Catarina, Trindade University Campus, Florianópolis, Santa Catarina 88040-900, Brazil

[b] Public Health Postgraduate Program, Federal University of Santa Catarina, Trindade University Campus, Florianópolis, Santa Catarina 88040-900, Brazil

[c] Medicine Course, Universidade do Sul de Santa Catarina, Pedra Branca Campus, Palhoça, Santa Catarina 88137-270, Brazil

[d] Bernard Lown Scholar in Cardiovascular Health, Department of Global Health and Population, Harvard T.H. Chan School of Public Health, Boston, USA

ARTICLE INFO

Keywords:
25(OH)D serum concentration
Cardiometabolic risk factors
Cross-sectional study
Cardiovascular diseases
Diabetes mellitus

ABSTRACT

To investigate the association between deficient and insufficient serum concentrations of 25(OH)D and cardiometabolic risk factors (CMRF), considering that both conditions are important predictors of cardiovascular disease and diabetes mellitus. A cross-sectional study with a subsample of 526 older adults (63–93 years old) who participated in the second wave of the population-based longitudinal study *EpiFloripa Idoso*. The CMRF analyzed were abdominal obesity, high fasting glucose, high blood pressure, high triglycerides and high LDL-cholesterol. The exposure variable was 25(OH)D serum concentration (≤20 ng/mL = deficient; 21–29 ng/mL = insufficient, ≥30-<100 ng/mL = sufficient). The prevalences of 25(OH)D deficiency and insufficiency were estimated at 21.9% and 43.7%, respectively. The adjusted OR of prevalence of the abdominal obesity (OR 1.99;1.12–3.54), high blood pressure (OR 2.58;1.35–4.94) and high LDL-cholesterol (OR 2.73;1.63–4.6) were higher among those with deficient serum concentration of 25(OH)D. Participants with insufficient serum concentrations of 25(OH)D also presented higher adjusted OR of prevalence for abdominal obesity (OR 2.14;1.31–3.48). No significant adjusted association was found between 25(OH)D with the outcomes high fasting glucose and high triglycerides. Significant effect modification/interaction by age was also observed in the tested associations for abdominal obesity ($P < 0.001$), blood pressure ($P < 0.001$) and LDL-cholesterol ($P < 0.001$), in which deficient and insufficient 25(OH)D values were associated with higher values of these FRCM. 25(OH)D serum concentrations between 30 and 100 ng/mL can contribute to preventing and controlling CMRF such as abdominal obesity, high blood pressure and high LDL-cholesterol. The understanding this particular interaction may indicate ways to prevent/control cardiometabolic outcomes, health problems common in the older adults.

1. Introduction

The segment of people aged 60 and over has been grown rapidly worldwide when compared to other age groups of the population and it is expected to more than triple by the end of this century, from 962 million in 2017 to three billion in 2100 (United Nations, 2015; United Nations, 2017). In the global south, more specifically in Brazil, it is estimated that in 2060 the country will have one of the largest elderly populations in the world, alongside countries like China, India and United States (Brazilian Institute of Geography and Statistics, 2020). The increase in the number of older adults in the country since 1970 has contributed to changing the Brazilian epidemiological scenario, which is currently marked by a high burden of morbidity and mortality from non-communicable diseases (NCDs), with emphasis on cardiovascular diseases and diabetes mellitus (Information Technology at the Service of the Health System, 2020; Malta et al., 2014).

In this scenario, the role of some classic risk factors for such diseases (physical inactivity, smoking, alcohol consumption and poor diet

* Corresponding author.
E-mail addresses: francieli.cembranel@ufsc.br (F. Cembranel), alexandra.boing@ufsc.br (A.C. Boing), antonio.boing@ufsc.br (A.F. Boing), andre.xavier@unisul.br (A.J. Xavier), eleonora.dorsi@ufsc.br (E. d'Orsi).

https://doi.org/10.1016/j.pmedr.2021.101587
Received 17 April 2021; Received in revised form 25 September 2021; Accepted 3 October 2021
Available online 7 October 2021

quality) is already well established, but by themselves they cannot explain the etiology or the greatest risk for all cases of cardiovascular disease and diabetes mellitus (cardiometabolic outcomes) (Malta et al., 2014; World Health Organization, 2003; World Health Organization, 2018). In the quest to define more proximal factors, recent researches have been dedicated to investigating the role of some cardiometabolic risk factors (CMRF) (abdominal obesity, high fasting glucose, high blood pressure, high triglycerides and high LDL-cholesterol) in the occurrence of cardiovascular disease and diabetes mellitus, as well as the effect of 25 (OH)D serum concentration on such CMRF (Autier et al., 2014; Jorde et al., 2010; Parker et al., 2010; Vitezova et al., 2015). A common hypothesis behind all these studies is that an increased prevalence of all CMRF mentioned has been consistently found in the elderly samples with insufficient (<30 ng/mL) and especially deficient (≤20 ng/mL) serum concentrations of 25(OH)D. According to the literature (Cheng et al., 2010; Kong and Li, 2006; Vitezova et al., 2015), when below 20 ng/mL, the 25(OH)D serum concentration has been related with accumulation of visceral fat, which promote increase in anthropometric measurements such as waist circumference, increase in blood glucose and in lipid profile indicators, in addition to promoting changes in the renin-angiotensin system, increasing the likelihood of high blood pressure, these conditions that together or alone predispose to cardiometabolic outcomes. Considering that both, the 25(OH)D serum concentration and the mentioned CMRF are modifiable factors, understanding this particular interaction may indicate ways for the prevention/control of cardiovascular diseases and diabetes mellitus in populations elderly.

In light of this, this study aimed to investigate the association between deficient and insufficient 25(OH)D serum concentrations and CMRF between older adults living in a capital city located in the south of Brazil. Additionally, in order to identify whether these associations are influenced by age due to a decrease in 25(OH)D with aging (MacLaughlin and Holick, 1985), this study also evaluated the modification of the effect by age in the tested associations.

2. Materials and method

2.1. Study design, population and location

Cross-sectional study with data from a subsample of 526 older adults (63–93 years old) who participated in the second wave (2013–2014) of the population-based longitudinal study *EpiFloripa Idoso*. The *EpiFloripa Idoso* had its first wave realized in 2009–2010, which was planned to investigate life conditions and general health among older adults of the Florianópolis. Florianópolis is the capital of a state located in the South of Brazil, nationally known for its low illiteracy rate (2.1%) and for having the third best Municipal Human Development Index in the country (HDI-M = 0.847) (United Nations Development, 2010).

2.2. Sample and sampling

The sample size of the *EpiFloripa Idoso* at the baseline (2009–2010) was calculated considering: reference population of 44,460 older adults (≥60 years), prevalence of 50% for unknown outcomes, sample error of 4.0 percentage points, 95% confidence interval (95% CI), design effect of 2.0, percentage for losses of 20%, and an additional 15% to adjustments in the association analysis, thereby generating an estimated sample of 1599 older adults. Considering the availability of financial resources and interviewers for fieldwork, the sample size was expanded to 1911 individuals.

The sampling was carried out by clusters in two stages. In the first stage, 80 of the 420 urban census sectors in Florianópolis were systematically selected according to the average monthly income of the head of the family (R$314.8-R$5,057.8; the equivalent of US$185,2-US $2,975.2; in 2009 US$1.00 equal to R$1.70). In the second stage, households were selected (an average of 102 people in the age group of interest were identified by census tract). All the older adult residents in the selected households were considered eligible, except those institutionalized or with limitations which interfered in obtaining anthropometric measurements. Thus, 1705 older adults were effectively interviewed in 2009–2010.

In 2013–2014 (second wave) 1197 participants from the original cohort were located and interviewed at their homes, and of these, a subsample of 604 older adults attended the facilities of the Federal University of Santa Catarina (UFSC) to collect biological samples (Fig. 1).

Additional details on the methodological aspects of the *EpiFloripa Idoso* can be consulted in previous publications (Confortin et al., 2017; Confortin et al., 2019; Schneider et al., 2017).

2.3. Ethical aspects

The longitudinalstudy*EpiFloripa Idoso* - was approved by the UFSC Ethics Committee on Human Research in both waves (protocol 352 in 2008; CAAE 16731313.0.0000.0121 in 2013).

3. Study variables

3.1. Outcomes

Five CMRF were considered as outcomes:

1. *Abdominal obesity*: this outcome was generated from the average of two waist circumference measurements (cm), which were obtained following standard procedure described in the literature (Lohman et al., 1988) and categorized according to cut-off points established by the World Health Organization (2008): waist circumference <88 cm in women and <102 cm in men = absence of abdominal obesity; waist circumference ≥ 88 cm in women and ≥102 cm in men = abdominal obesity.

2. *High blood pressure*: this variable was generated from a combination of measured values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) and categorized according to cut-off points proposed by the International Society of Hypertension (Unger et al., 2020) and the 7th Brazilian Guideline on Hypertension (Brazilian Society of Cardiology, 2016): SBP <140 mmHg and DBP <90 mmHg = normal blood pressure; SBP ≥140 mmHg and/or DBP ≥90 mmHg = high blood pressure. Both blood pressure measurements were obtained from the left arm after each participant remained at rest for at least 10 minutes.

3. *High fasting glucose*: this variable was generated from laboratory values of fasting glucose (mg/dL) and categorized according to cut-off points established by the American Diabetes Association (American Diabetes Association, 2019): fasting glucose <100 mg/dL = normal fasting glucose levels; fasting glucose ≥100 mg/dL = high fasting glucose levels.

4. *High triglycerides*: this variable was generated from laboratory values of fasting triglycerides (mg/dL) and categorized according to cut-off points of the American College of Cardiology (Jacobsen et al., 2019) and the Brazilian Society of Cardiology (Brazilian Society of Cardiology, 2017): triglycerides <150 mg/dL = normal triglyceride levels, triglycerides ≥150 mg/dL = high triglyceride levels.

5. *High LDL-cholesterol*: this variable was generated from laboratory values of fasting LDL-cholesterol (mg/dL) and categorized according to cut-off points of the American College of Cardiology (Reiter-Brennan et al., 2020) and the Brazilian Society of Cardiology (Brazilian Society of Cardiology, 2017): LDL-cholesterol <100 mg/dL = normal LDL-cholesterol levels, LDL-cholesterol ≥100 mg/dL = high LDL-cholesterol levels.

3.2. Exposure

The exposure was 25(OH)D serum concentration in three categories: deficient (≤20 ng/mL), insufficient (21–29 ng/mL) and sufficient

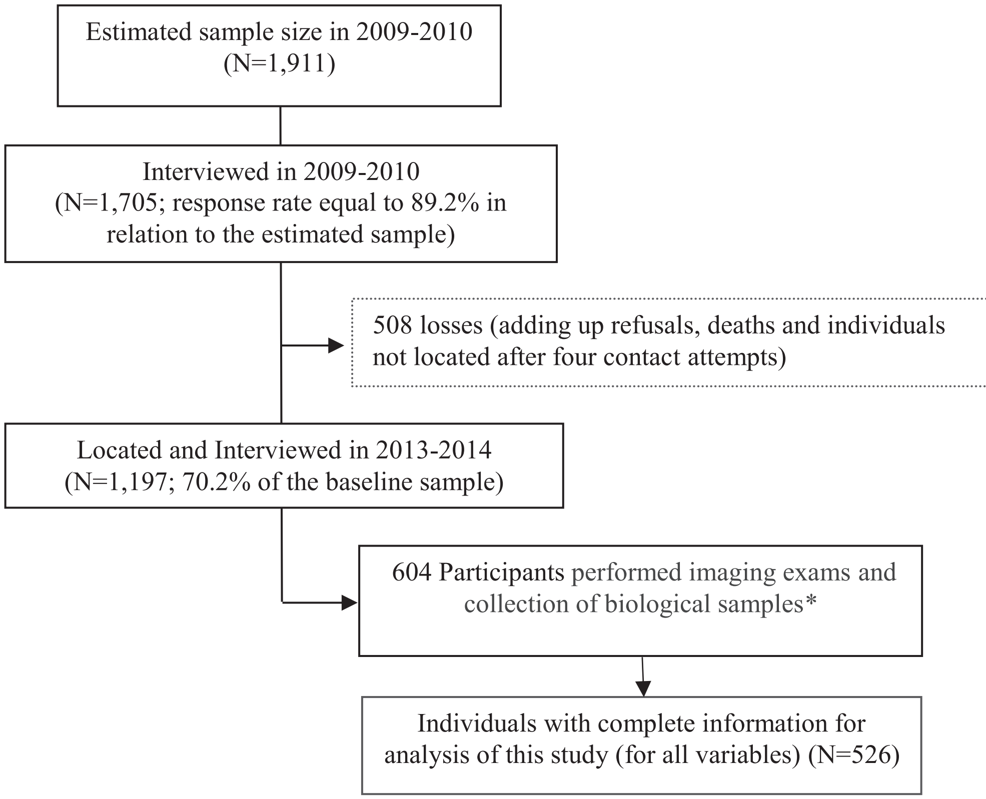

Fig. 1. Flowchart of the follow-ups (2009–2010 and 2013–2014). Longitudinal study *EpiFloripa Idoso*. Florianópolis, Santa Catarina, Brazil.

(≥30–<100 ng/mL) (Sempos and Binkley, 2020). Microparticle chemiluminescent method was used to determine 25(OH)D serum concentration in blood samples, which were collected from the participants after 8–12 h of fasting, following the protocol of the UFSC University Hospital Laboratory for collection, storage (-80 °C) and dosage (Prado and Gelbcke, 2013).

3.3. Co-variables

In agreement with the literature (Autier et al., 2014; Jorde et al., 2010; Parker et al., 2010; Vitezova et al., 2015) were considered covariates in this study: sex (female, male), age (full years at the time of the interview), skin color (white, others), family income per capita in reais (R$ Brazilian currency = US$1.00 equivalent to R$1.70 in 2009 and R $2.16 in 2013), schooling in full years of study, tobacco (never smoked, smoked and quit/currently smokes), alcohol (never consumes, moderate/high consumption) and leisure and commuting physical activity (in weekly minutes). These variables were obtained through a questionnaire, in a face-to-face interview at the participants' homes. The questionnaires were pre-tested, the interviewers trained and standardized for the quality control of the variables obtained in both study waves.

3.4. Data analysis

All analyses were conducted in the Stata software version 14.0 (StataCorp®, Bryan, TX, USA) using sample weights, which were determined considering the effect of the sample design at the baseline and the location probability of the participants in the second wave according to each census sector (cluster). These sample weights were further recalculated for the estimated population of Florianópolis in 2013 and for the number of subjects who participated in the biological marker collection in 2013–2014.

Chi-Squared test with Rao-Scott correction (Rao and Scott, 1981) was used to describe the categorical variables (%), while to describe the continuous variables the data were expressed as means with their respective standard deviations or as medians and interquartile ranges.

Logistic Regression was used to estimate the strength of the association between the 25(OH)D categories and each CMRF. Two analysis models were performed: Crude Logistic Regression (crude OR) and Adjusted Logistic Regression (adjusted OR) for all co-variables.

Heterogeneity tests for the age (63–69, 70–79, 80 years or more) were also performed, considering as indicative of interaction/effect modification values of $p \leq 0.10$. The results of this analysis using Adjusted Linear Regression were presented graphically.

4. Results

The data for the cross-sectional analyzes of this study came from the participants of the cohort study *EpiFloripa Idoso* (2013–2014 wave) with complete information for all variables of interest (N = 526). We believe that it is unlikely that this reduced sample size could have biased the results found, considering that the sociodemographic characteristics remained in a similar percentage between 2009–2010 and 2013–2014, except income (increased) (Table 1). In this sample, the prevalences of 25(OH)D deficiency and insufficiency were estimated at 21.9% and 43.7%. The prevalences of abdominal obesity, high fasting glucose, high blood pressure, high triglycerides and high LDL-cholesterol among those with 25(OH)D deficiency were 26.5%, 19.5%, 25.0%, 28.5% and 26.2%, respectively (Table 2).

Table 3 presents the results of the crude and adjusted associations between the 25(OH)D serum concentrations and each CMRF. The OR of prevalence for abdominal obesity in the crude analysis was 2.44 (1.53–3.91) and 2.13 (1.22–3.7) times higher among individuals with insufficient and deficient 25(OH)D serum concentrations, respectively. After adjustment, the strength of the association remained similar, with a OR of prevalence for abdominal obesity equal to 2.14 (1.31–3.48) and 1.99 (1.12–3.54), respectively for those with insufficient and deficient 25(OH)D serum concentrations. Similar results have also been identified

Table 1
Comparison of the sample characteristics between the baseline (2009–2010) and the follow-up in 2013–2014. Longitudinal study *EpiFloripa Idoso*, Florianópolis, Brazil.

Characteristics	Interviewed in 2009–2010 (N = 1705)	Interviewed in 2013–2014* (N = 604)	Individuals with complete information for analysis of this study (for all variables) (N = 526)
Sex (female) – %	63.9	65.2	64.8
Age (years) – Mean ± SD	70 ± 8	72 ± 6.4	72 ± 6.2
Skin color (white) – %	85.3	83.9	83.7
Education level (years of study) – Mean ± SD	7.6 ± 5.7	7.9 ± 5.7	7.9 ± 5.8
Family income (per capita. in R$) – Median (p25–p75)	730 (350–1500)	1200 (720–2500)	1220 (720–2600)
Tobacco use (smoked and stopped/ currently smokes) – %	39.0	37.3	36.7
Alcohol consumption (moderate/high consumption) – %	35.0	41.7	43.0
Leisure and commuting physical activity (weekly minutes‡) – Mean ± SD	**	280 ± 310	290 ± 310
Abdominal obesity (waist circumference ≥88 cm in women and ≥102 cm in men) – %	53.3	55.8	54.6
High fasting glucose (≥100 mg/dL) – %	**	39.9	39.5
High blood pressure (systolic ≥140 mmHg and/or diastolic ≥90 mmHg) – %	**	58.8	57.8
High triglycerides (≥150 mg/dL) – %	**	26.6	26.1
High LDL-cholesterol (≥100 mg/dL) – %	**	68.2	67.3
25(OH)D – Mean ± SD	**	26 ± 9	27 ± 9

SD = Standard deviation.
R$ = Brazilian currency (US$1.00 equivalent to R$1.70 in 2009, and R$2.16 in 2013).
p25-p75 = interquartile range.
* = Individuals interviewed in 2013–2014 who performed blood tests.
** = Data not collected between the baseline sample.
‡ = variable obtained using the international physical activity questionnaire (IPAQ) (Hagstromer, M., Oja, P., Sjostrom, M., 2006. The international physical activity questionnaire (IPAQ): a study of concurrent and construct validity. Public Health Nutr. 29:755–62).

for high blood pressure and high LDL-cholesterol in the adjusted analysis. The OR of prevalence was equal 2.58 (1.35–4.94) for high blood pressure and 2.73 (1.63–4.6) for LDL-cholesterol for those with deficient 25(OH)D serum concentrations when compared to those with 25(OH)D serum concentrations ≥30.0–100 ng/mL. No significant adjusted association was found between 25(OH)D with the outcomes high fasting glucose and high triglycerides.

Regarding the effect modification by age, significant results of heterogeneity were observed in the associations between 25(OH)D serum concentrations and abdominal obesity, blood pressure and LDL-cholesterol outcomes (Fig. 2). For the three age groups under analysis,

Table 2
Distribution of sample characteristics according to 25(OH)D serum concentration categories. Longitudinal study EpiFloripa Idoso (2013–2014 wave), Florianópolis, Brazil.

Characteristics	≤20 ng/mL (N = 115)	20–29 ng/mL (N = 230)	≥30 to <100 ng/mL (N = 181)	*p-value*
Sample – %	21.9	43.7	34.4	<0.001
Age (years) – Mean ± SD	73 ± 6	72 ± 6	71 ± 6	0.04
Skin color (white) – %	21.4	42.5	36.1	0.57
Education level (years of study) – Mean ± SD	7.7 ± 4.6	7.9 ± 5.9	9.3 ± 6.3	0.03
Family income (per capita. in R$) – Mean ± SD	2000 ± 2300	2400 ± 2800	3000 ± 4000	0.03
Tobacco use (smoked and stopped/ currently smokes) – %	22.3	40.9	36.8	0.59
Alcohol consumption (moderate/ high consumption) – %	20.4	44.3	35.4	0.76
Leisure and commuting physical activity (weekly minutes‡) – Mean ± SD	200 ± 230	250 ± 260	410 ± 360	<0.001
Abdominal obesity (waist circumference ≥88 cm in women and ≥102 cm in men) – %	26.5	48.1	25.4	<0.001
High fasting glucose (≥100 mg/dL) – %	19.5	43.1	37.3	0.12
High blood pressure (systolic ≥140 mmHg and/or diastolic ≥90 mmHg) – %	25.0	43.1	31.9	0.10
High triglycerides (≥150 mg/dL) – %	28.5	43.8	27.7	0.048
High LDL-cholesterol (≥100 mg/ dL) – %	26.6	44.4	29.1	<0.001

SD = Standard deviation.
R$ = Brazilian currency (US$1.00 equivalent to R$1.70 in 2009, and R$2.16 in 2013).
* = Individuals interviewed in 2013–2014 who performed blood tests.
‡ = variable obtained using the international physical activity questionnaire (IPAQ) (Hagstromer, M., Oja, P., Sjostrom, M., 2006. The international physical activity questionnaire (IPAQ): a study of concurrent and construct validity. Public Health Nutr. 29:755–62).

lower 25(OH)D values (equivalents with deficiency and insufficiency) were associated with higher values of the waist circumference, blood pressure and LDL-cholesterol (p-value of the heterogeneity test of model <0.001 for the three outcomes), being the modifying effect of age in these associations even more expressive for the younger group (63–69 years), when compared to those aged 70–79 and 80 years of age or older. At every 10 ng/mL increase in the serum concentration of 25(OH)D, was observed a reduction of 0.15 cm in waist circumference, 0.13 mmHg in blood pressure and of 0.59 mg/dL in LDL-cholesterol. For the intermediate age group (70–79) and 80 years or older, these values were respectively −0.08 cm, −0.25 mmHg, −0.02 mg/dL, and −0.1 cm, −0.03 mmHg, −0.01 mg/dL. For the fasting glucose and triglyceride outcomes, the results of the heterogeneity tests were not significant (p-value >0.10).

5. Discussion

Two main findings can be highlighted from this investigation: first, the adjusted OR of prevalence of abdominal obesity, high blood pressure and high LDL-cholesterol were higher among older adults with deficient 25(OH)D serum concentration when compared to those with sufficient serum concentrations. Second, consistent results of heterogeneity were observed in the associations between 25(OH)D serum concentrations and abdominal obesity, blood pressure and LDL-cholesterol, when the analyzes were stratified by age groups.

Such findings are consistent with results from previous studies in the scientific literature (Autier et al., 2014; Jorde et al., 2010; Parker et al.,

Table 3
Crude and adjusted* odds ratio between the 25(OH)D serum concentrations and cardiometabolic risk factors (CMRF). Longitudinal study *EpiFloripa Idoso* (2013–2014 wave), Florianópolis, Brazil.

25(OH)D serum concentration (exposure)†	Crude OR (95%CI)	Adjusted OR (95%CI)
(outcomes)		
Abdominal obesity (WC ≥88 cm in women and WC ≥102 cm in men)		
p-value	*<0.001*	*0.004*
≤20 ng/mL – deficient	2.13 (1.22–3.7)	1.99 (1.12–3.54)
21–29 ng/mL – insufficient	2.44 (1.53–3.91)	2.14 (1.31–3.48)
≥30 to <100 ng/mL – sufficient	Ref.	Ref.
High blood pressure (SBP ≥140 mmHg and/or DBP ≥90 mmHg)		
p-value	*0.04*	*0.02*
≤20 ng/mL – deficient	2.43 (1.21–4.88)	2.58 (1.35–4.94)
21–29 ng/mL – insufficient	1.24 (0.78–1.97)	1.31 (0.81–2.1)
≥30 to <100 ng/mL – sufficient	Ref.	Ref.
High fasting glucose (≥100 mg/dL)		
p-value	*0.049*	*0.10*
≤20 ng/mL – deficient	1.89 (0.91–9.96)	1.75 (0.82–3.72)
21–29 ng/mL – insufficient	1.72 (1.07–2.76)	1.67 (1.01–2.76)
≥30 to <100 ng/mL – sufficient	Ref.	Ref.
High Triglycerides (fasting triglycerides ≥150 mg/dL)		
p-value	*0.19*	*0.26*
≤20 ng/mL – deficient	1.7 (0.89–3.25)	1.61 (0.79–3.29)
21–29 ng/mL – insufficient	1.13 (0.67–1.93)	1.05 (0.6–1.87)
≥30 to <100 ng/mL – sufficient	Ref.	Ref.
High LDL-cholesterol (≥100 mg/dL)		
p-value	*0.002*	*<0.001*
≤20 ng/mL – deficient	2.8 (1.6–4.9)	2.73 (1.63–4.6)
21–29 ng/mL – insufficient	1.4 (0.81–2.43)	1.27 (0.74–2.17)
≥30 to <100 ng/mL – sufficient	Ref.	Ref.

WC = Waist Circumference.
SBP = Systolic blood pressure measured in the left arm.
DBP = Diastolic blood pressure measured in the left arm.
25(OH)D serum concentration = Serum concentration of vitamin D in ng/mL.
Ref. = Reference category (25(OH)D ≥30-<100 ng/mL – sufficient.
* Adjusted association for sex, age (continuous), skin color, per capita family income (continuous), educational level, alcohol, smoking and leisure and commuting physical activity (continuous).
† In the study sample, no participant had 25(OH)D values above 100 ng/mL (mean 26.4 ng/mL; standard deviation 9.1 ng/mL; Minimum – Maximum: 4–96.8 ng/mL).

2010; Vitezova et al., 2015) and can be explained by several mechanisms (Jeong et al., 2017; Kong and Li, 2006; Vitezova et al., 2015). First, 25(OH)D serum concentrations when below 20 ng/mL inhibit the differentiation of adipocytes and can thus influence the development of abdominal obesity. In addition, insufficient and/or deficient values promote an increase in parathyroid hormone (PTH), which is known to favor the lipid storage in the body. Third, the active form (serum 1,25-dihydroxyvitamin D) acts as a suppressor of the renin-angiotensin system favoring the elevation of pressure levels. Fourth, added to this scenario the fact that there is a progressive decrease with the advancing age in the amount of pre-vitamin D3 and 7-dehydrocholesterol, the main precursors of 25(OH)D serum concentration (85–90% of vitamin D synthesis occurs in the dermis). According to MacLaughlin and Holick (1985), while the amount of pre-vitamin D3 in the dermis at 8 years of age is estimated to be 36 ng/cm^2, this value decreases to 24 ng/cm^2 at 77, and it becomes only 20 ng/cm^2 at 82 years of age. Likewise, the amount of 7-dehydrocholesterol decreases from 1800 ng/cm^2 at 8 years of age to 1630 ng/cm^2 and 1040 ng/cm^2 at 77 and 82 years of age, respectively. These findings may even help to understand the high prevalence of vitamin D deficiency in elderly populations from different countries: 61% in United States, 67% in Iran, 72% in Pakistan, 90% in Turkey and 96% in the India (Sizar et al., 2021). In Brazil, despite the absence of national data on deficiency prevalence of D vitamin by the serum concentration, data from the National Food Survey (INA) for older adults show an inadequate vitamin D intake prevalence by the diet equal 98.9% (Fisberg et al., 2013).

In light of these hypotheses and numbers, it is easy to understand the influence of low serum concentrations of 25(OH)D on the manifestation of CMRF under study, and consequently the high prevalence of cardiometabolic outcomes worldwide.

According to data from the WHO published in 2018, cardiovascular disease (17.9 million) and diabetes (1.6 million) together are responsible for approximately 31% of the total deaths from NCDs in the world. Data from the same study still show an important disproportionality in the occurrence of NCDs when comparing high-income countries with low and middle-income countries (LMICs). It is estimated that 80% (32 million) of the total annual deaths in the world by NCDs occur in LMICs (World Health Organization, 2018). Specifically for Brazil, data from Information Technology at the Service of the *Sistema Único de Saúde* (DATASUS) show that of the total deaths registered in the country in 2013 (1,210,474), 829,916 deaths were due to NCDs. Cardiovascular diseases (29.7%) and diabetes (5.1%) alone was responsible for more than a third of this total number of deaths (Malta et al., 2019).

For the authors such as Beaglehole et al. (2011), Dieleman et al. (2016), Heller et al. (2019) and Horton (2015) these high numbers may be the result of low global financial political investment in the prevention of NCDs. In Brazil, the cardiovascular diseases alone were responsible for a deficit on economy of US$ 4.18 billion between 2006 and 2015 due to family expenses on treatment and the impact on productivity (Malta et al., 2019). In the European Union, cardiovascular disease is estimated cost the country economy €210 billion in the year in 2015, of which 53% (€111 billion) was due to healthcare costs, 26% (€54 billion) to productivity losses and 21% (€45 billion) to the informal care of people with CVD (Timmis et al., 2020).

In this scenario, it is still necessary to consider that mortality rates by NCDs increase significantly with increasing age. According to a study in the United States (Xu, 2019), the number of deaths in people between 65 and 74 years of age can be up to eight times higher than in young adults aged 35–44 years. A second study in the United States with data from the National Health and Nutrition Examination Survey (NHANES) (Al-Khalidi, Kuk, Ardern, 2019) shows additionaly that mortality from cardiometabolic diseases (cardiovascular disease, diabetes mellitus and cerebrovascular disease) in subjects with mean age of 61 years (±13.9) can be twice as high among those with 25(OH)D serum concentrations under 12 ng/mL.

Given the presented findings, the paper of vitamin D on the investigated outcomes is evident. However, considering that neither regular exposure to the sun and/or food intake are sufficient to provide adequate 25(OH)D serum concentrations in elderly populations (Bruins et al., 2019; Fisberg et al., 2013; MacLaughlin and Holick, 1985), a possible way out of reversing this scenario could focus on vitamin D supplementation. But, in practice, results of studies which have evaluated the effect of supplementing this vitamin on CMRF are controversial. For example, in a review study conducted by Jeong et al. (2017) and in a meta-analysis conducted by Zhang et al. (2020) did not identify any benefits of vitamin D supplementation in the individual treatment of hypertension or even for an intervention at a population level. On the other hand, the studies conducted by Davidson (2021) and Mirhosseini et al. (2018) suggests benefits of vitamin D supplementation on CMRF such as high blood pressure, high fasting glucose and high LDL-cholesterol. However, the authors of this studies emphasize that the benefits of supplementation were only observed when the 25(OH)D serum concentration reached values equal to or greater than 34.4 ng/mL (Mirhosseini, Rainsbury, Kimball, 2018). In the face of this inconsistences, our study recommends that the increase in 25(OH)D serum concentration occur by diet (greater consumption of source foods) as well as by exposure to the sun (5–30 min, two to three times a week between the times of 10 am to 3 pm). Is that studies have shown that the simple exposure of some areas of the body (hands, arms and face) to the sun that produces a minimal erythema , is equivalent to a dietary intake of 1000 international units (IU) of vitamin D (Brazilian Society of Dermatology, 2013; Engelsen, 2010; Saternus et al., 2019), a higher

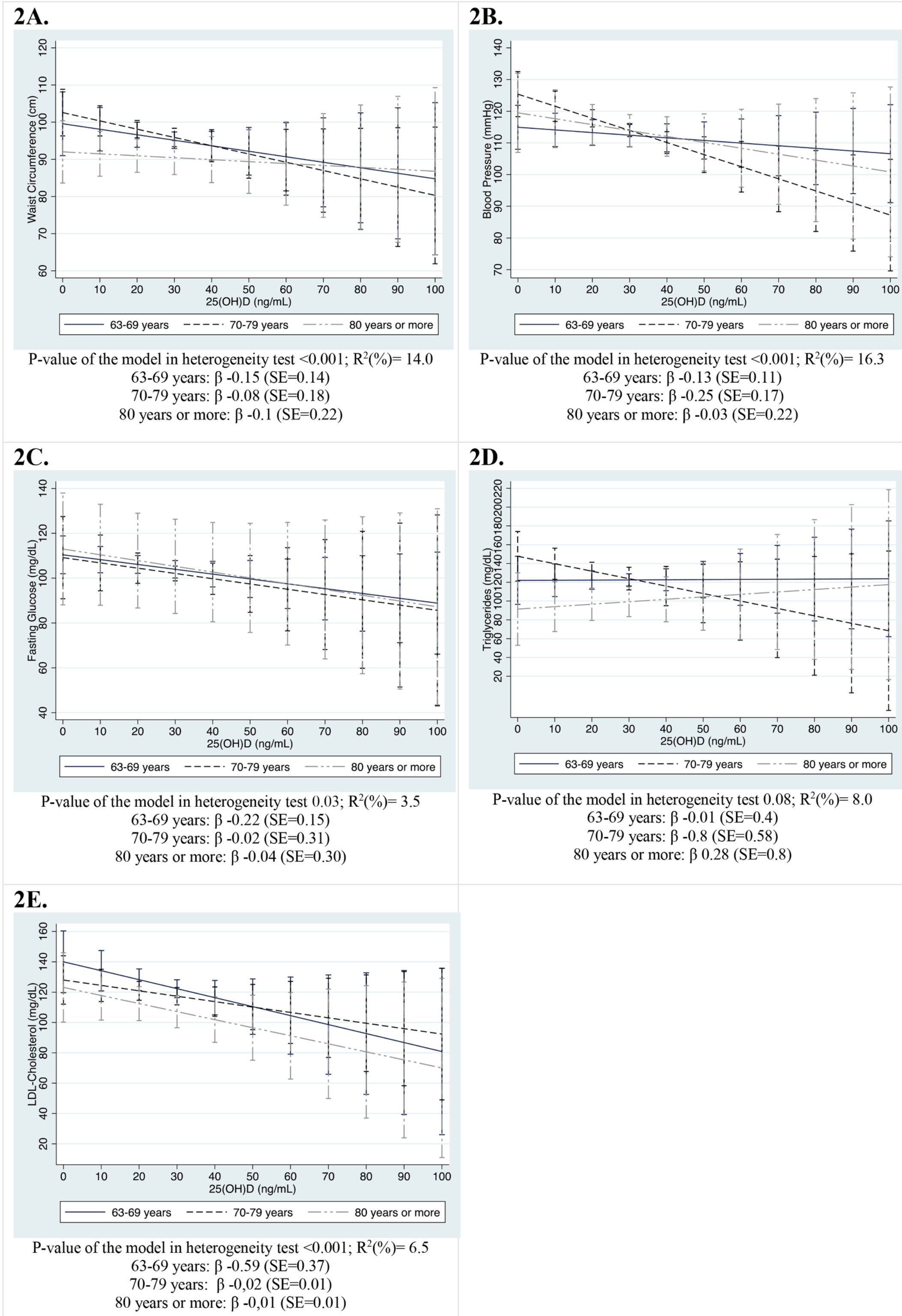

Fig. 2. Figures of the Linear Regression* between the 25(OH)D status and cardiometabolic risk factors (CMRF), adjusted for sex skin color, per capita family income (continuous), educational level (continuous), alcohol consumption, smoking and leisure and commuting physical activity (continuous), stratified by age. Longitudinal study *EpiFloripa Idoso* (2013–2014 wave), Florianópolis, Brazil.

value than that recommended by the Recommended Dietary Allowances (RDA) (Institute of Medicine, 2011), which is 600 IU/day for individuals aged 51–70 years and 800UI/day for those over 80 (by diet).

Regarding limitations of the present study, we highlight the fact that this study has a cross-sectional design, which limits determining causality in the tested associations. Another limitation of this study refers to the non-inclusion of variables related to the use of medication to treat CMRF in the adjusted analyses, considering that these variables were not collected in the 2013–2014 wave. Data on dietary intake of vitamin D and/or supplement use, which could possibly influence the serum concentration of this vitamin were also not considered in the analyzes because they were not collected. The confounding effect of the body mass index (BMI) was not also taken into account in the analyzes of this study, because for authors like Al-khalidi, Kuk and Ardern (2019) who recently studied the risk of mortality in a sample of 7,958 individuals from NHANES, the relationship between 25(OH)D serum concentration and the risk of mortality from cardiometabolic diseases is independent of BMI. Regarding the study strengths, we highlight the stratification of the association analyzes by age groups, considering that the modification of the effect promoted by age has not yet been explored by previous studies in the scientific literature.

6. Final considerations

With population aging, mortality rates from NCDs – especially from diabetes and cardiovascular disease – tend to considerably increase. Therefore, monitoring progress, as well as the risk factors for such diseases can be an important strategy to guide public health decision-making. For the WHO, preventively intervening on such problems can even be an excellent economic investment for countries due to the financial impact of these diseases on productivity, family/individual budgets and the public health systems (World Health Organization, 2018). In this scenario, public health strategies which contribute to reversing vitamin D deficiency are necessary, since the results of this and other previous studies, place this vitamin as an important modifiable risk factor to prevention and control of CMRF and therefore of NCDs. According to current scientific evidence, it is important to emphasize that elevation 25(OH)D serum concentrations must occur by increasing regular exposure to the sun and by ingesting this nutrient in the diet, instead of by supplementation until they have a consolidated protocol for this purpose.

CRediT authorship contribution statement

Francieli Cembranel: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Visualization, Writing – original draft, Writing – review & editing. **Alexandra Crispim Boing:** Visualization, Writing – original draft, Writing – review & editing. **Antonio Fernando Boing:** Visualization, Writing – original draft, Writing – review & editing. **André Junqueira Xavier:** Visualization, Writing – review & editing. **Eleonora d'Orsi:** Data curation, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Participants, the Brazilian National Council for Scientific and Technological Development (*Conselho Nacional de Desenvolvimento Científico e Tecnológico* – CNPq) for financial support of the cohort study *EpiFloripa Idoso* in the 2013-2014 wave, and the Public Health Postgraduate Program of Federal University of Santa Catarina.

Financial support

This article was elaborated with data from the longitudinal longitudinal study *EpiFloripa Idoso* known as "*Estudo Epidemiológico das Condições de Saúde dos Idosos de Florianópolis, Santa Catarina, Brasil*", 2013-2014 wave, financed by the CNPq, process numbers 475904/2013-3 in the amount of R$59,926.60, equivalent to US$27,743.80 (US$1.00 equivalent to R$2.16, in 2013).

Ethical approval

All the participants gave their consent prior to inclusion in the study. All data were recorded anonymously. The longitudinal study *EpiFloripa Idoso* was approved by the Federal University of Santa Catarina (UFSC) Ethics Committee on Human Research in both waves (protocol n^{o}. 352 in 2008; and CAAE 16731313.0.0000.0121 in 2013), according to the guidelines laid down in the Declaration of Helsinki.

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