ORIGINAL ARTICLE

Components of frailty, sarcopenia and their association with vitamin D insufficiency. Analytical cross-sectional study

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Resume

Introduction: In older adults, the association of frailty and sarcopenia with vitamin D deficiency is known, but little has been studied about the association of the components of the frailty syndrome. **Objective:** To determine the association between the components of frailty, sarcopenia and vitamin D insufficiency in older adults. **Methods:** Adults were studied. Age, education, marital status, history of fractures, hospitalizations, anthropometric indicators, sarcopenia, Charlson index, polypharmacy, Fried's frailty phenotype, and plasmatic vitamin D were recorded. Figures <30 ng/mL were considered indicative of vitamin D insufficiency. Descriptive and inferential statistics were used for the statistical analysis. The association was determined by binary logistic regression. **Results:** 175 adults with a mean age of 71.7 ± 6.7 years (95% CI = 60-90 years) were studied. Binary logistic regression showed that the variables associated with vitamin D insufficiency were depletion (OR = 2.6, 95% CI = 1.0-6.5, p = 0.03), frailty (OR = 9.2, 95% CI = 2.5-34.1, p = 0.001) and pre-frailty (OR = 4.6, 95% CI = 2.1-10.0, p < 0.001). **Conclusion:** The frail, pre-frail and exhaustion phenotypes are associated with vitamin D insufficiency.

KEY WORDS: Older adult. Fragility. Insufficiency. Sarcopenia. Vitamin D.

Components of frailty, sarcopenia and their association with vitamin D deficiency. Cross-sectional, analytical study

Abstract

Introduction: In older adults, the association of frailty and sarcopenia with vitamin D deficiency is well known, but the asso ciation of the components of frailty syndrome has been poorly studied. **Objective:** To determine the association of the com ponents of frailty and sarcopenia with vitamin D insufficiency in older adults. **Methods:** Adults were studied, in whom age, education, marital status, history of fractures, hospitalizations, anthropometric indicators, sarcopenia, Charlson index, polyphar macy, Fried's frailty phenotype, and plasma vitamin D were recorded; figures < 30 ng/mL were considered indicative of vitamin D insufficiency. Descriptive and inferential statistics were used for statistical analysis. The association was determined by binary logistic regression. **Results:** One-hundred and seventy-five adults with a mean age of 71.7 ± 6.7 years (95% CI = 60-90 years) were studied. Binary logistic regression showed that the variables associated with vitamin D deficiency were exhaustion

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KEYWORDS: Older adult. Frailty. Insufficiency. Sarcopenia. Vitamin D.

Introduction

Frailty is a state of vulnerability that is associated with mortality, disability, and hospitalization.1 Sarcopenia is frequently associated with frailty and is mainly due to the progressive and generalized loss of strength and muscle mass.2,3 Previous reports have shown that vitamin D deficiency increases the levels of proinflammatory cytokines related to decreased muscle strength and physical performance.4-6 In older adults, the association of frailty and sarcopenia is known, but not the association of the latter with the components of frailty syndrome and vitamin D deficiency. The objective of this study was to analyze this relationship in older adults from western Mexico.

Methods

From February to September 2020, an analytical cross-sectional study was carried out. Older adults members of the Coexistence Center for the Third Age Regional Park, Colima, Mexico were selected. The inclusion criteria were age ÿ 60 years and attendance at the Center three or more times a week. Individuals with active calcitriol supplementation, acute illness of less than one month at the time of assessment, severe cognitive deficit, and inability to ambulate were excluded. Individuals with incomplete data or with an inadequate blood sample (haemolyzed or insufficient) were eliminated.

The study was authorized by the Bioethics Committee of the Faculty of Medicine of the University of Colima, with registration number R2017/3/2, and by the National System for the Integral Development of the Family of the state of Colima. The purpose of the study was explained to each participant and they were asked to sign an informed consent letter from accordance with the provisions of the Declaration of Helsinki modified in 2013 and the norms established by the Mexican General Health Law. The information collected was confidential.

Fragility

The state of fragility was determined with the Fried's five criteria:1

– Unintentional weight loss ÿ 5 kg or ÿ 5% of body weight in the past year.

– Weakness, assessed with a dynamometer, whose existence was considered when the grip strength of the dominant hand was less than the quintile adjusted for sex and body mass index.

– Feeling exhausted. The Depression Scale of the Center of Epidemiological Studies was used, with which exhaustion was considered when assenting to two or more of the following statements: "I feel exhausted", "I feel that I move very slowly", "I feel that everything I do it with a lot of effort", "I feel tired all the time".

– Slow walking. Gait was considered slow if it qualified with a <20th percentile adjusted for sex and height (<80 cm/second).

– Low activity. Questions were asked about the frequency of different activities (sports, work at home, walking). The activity criterion was met by those who responded one to three times a week; it was not fulfilled by those who responded never or almost never.

According to the number of criteria present, three grades were considered: – Frailty, ÿ 3 criteria.

– Pre-frailty, between one and two criteria.

– No fragility, without any criteria.

Sarcopenia

The criteria of the European Working Group on Sarcopenia in Older Adults updated in 2018 were used.3 The classification is made up of three criteria: – Low muscle strength, less than the lower quintile of grip strength (kg) of the dominant hand.

– Low quantity/quality of muscle, less than quintile lower from the muscle mass.

– Low physical performance, walking speed < 80 cm/second.

One criterion indicated probable sarcopenia; two criteria, sarcopenia; and three criteria, severe sarcopenia.

Vitamin D

25-dihydroxyvitamin D was determined in serum using the ELISA (enzyme-linked immunosor bent assay) method; the patient was considered to have failure if the value was <30 ng/mL and to have deficiency if the level was <20 ng/mL.

Other variables

Each participant underwent a clinical history in which identification data, sociodemographic data (age, sex, marital status, and years of schooling), history of chronic diseases, fractures, and hospitalizations, anthropometric indicators (weight, height, brachial, calf, waist and hip circumferences, as well as body mass index), systolic and diastolic blood pressure, modified Charlson comorbidity index

(ÿ 2), polypharmacy (ÿ 4 drugs) and serum hemoglobin.

Statistic analysis

Descriptive statistics were used as means and standard deviations for the quantitative variables. The means were compared with the Student's t or Mann-Whitney U tests and the percentages with the chi-square test.

Two binary logistic regression (BRL) models were performed to avoid collinearity or relationship between covariates.

– Model 1, all covariates were entered, including frailty syndrome components, and frailty and pre-frailty phenotypes were excluded.

– Model 2, all covariates were included, as well as frailty and pre-frailty phenotypes, and components of the frailty syndrome were excluded.

The input explanatory method and the forward likelihood ratio predictive method were used. The dependent variable was the level of vitamin D, with two cut-off points according to the figures:

– < 30 ng/mL, insufficiency + deficiency. – < 20 ng/mL, deficiency.

Finally, sarcopenia and its association with covariates was analyzed with forward selection-based RLB based on likelihood ratio.

In all tests, a 95% confidence interval (95% CI) was used and statistical significance was considered with $p < 0.05$.

Results

175 older adults (145 women and 30 men) with a mean age of 71.7 ± 6.7 years (95% CI = 60-90 years) were studied. The frequencies of pre-frailty and frailty were 51.4% (n = 90, 73 women and 17 men) and 18.9% (n = 33, 29 women and 4 men), respectively. There was no significant difference in the comparison of percentages of the phenotypes between men and women. Of the frailty criteria, the most frequent were low physical activity (42.4%, n = 74) and feeling exhausted (40%, n = 70).

The mean vitamin D was 27.9 ± 14.7 ng/mL. Vitamin insufficiency occurred in 41.1% (n = 72), deficiency in 34.2% (n = 60) and 24.5% (n = 43) presented normal figures.

Table 1 expresses the comparison of the means of the quantitative variables between the groups with figures of insufficiency/deficiency and normal values of vitamin D.

Insufficiency + vitamin D deficiency (n = 132)

In model 1, burnout was associated with the dependent variable (Table 2).

In model 2, it was observed that frailty and pre-frailty were associated with the dependent variable (Table 2).

In the RLB with forward selection based on the likelihood of the likelihood ratio, no association was identified between insufficiency + vitamin D deficiency, all covariates + syndrome components (pre-frailty and frailty phenotypes excluded).

In the LLR forward selection based on the likelihood of the ratio in which insufficiency + vitamin D deficiency all covariates + pre-frailty + frailty (excluding the components of the syndrome) were analyzed, the associated variables were frailty (odds ratio

Table 1. **Comparison of means, standard deviation and statistical significance between adults with and without vitamin D deficiency.**

Variable	Vitamin D		p*
	Insufficiency/ deficiency (n = 132)	Normal (n = 43)	
	Mean ± SD	Mean ± SD	
Age (years)	72.1 ± 6.8	70.4 ± 6.3	0.1
Size M)	1.56 ± 0.07	1.57 ± 0.05	0.2
Weight (kg)	70.5 ± 12.5	68.5 ± 11.7	0.4
IMC (kg/m2)	28.9 ± 4.6	27.7 ± 11.7	0.1
P twin (cm)	35.5 ± 3.9	35.1 ± 3.4	0.2
P braquial (cm)	31.1 ± 4.3	31.0 ± 3.7	0.8
P waist (cm)	93 ± 9.2	92.4 ± 9.6	0.4
P hip (cm)	104 ± 10	103 ± 9.2	0.4
Systolic pressure (mm Hg)	121.7 ± 13	120 ± 13.6	0.7
Diastolic pressure (mm Hg)	70.9 ± 10.2	68,7 ± 10.2	0.2
Drugs received (n)	2.8 ± 2.2	2.9 ± 2.5	0.8
Dominant hand dynamometry (kg)	19.8 ± 7.5	24.9 ± 9.9	0.03
Hemoglobin (g/dL)	12.6 ± 1.2	12.5 ± 1.3	0.9

kg/m2 = weight in kilograms divided by height in meters squared; Q: perimeter.
*t for Student.

[OR] = 3.9, 95% CI = 1.1-13.5, p = 0.02), pre-frailty (OR = 2.4, 95% CI = 1.2-5.0, p = 0.01), sarcopenia (OR = 2.7, 95% CI = 1.1-22.0, p = 0.01) and overweight (OR = 0.4, 95% CI = 0.2-0.9, p = 0.03).
In the multivariate analysis with MR adjustment, the associated variables were frailty (OR = 9.2, 95% CI = 2.5-34.1, p = 0.001) and pre-frailty (OR = 4.6, 95% CI = 2.1-10.0, p < 0.001).

Vitamin D deficiency (n = 60)

There was no association of the covariates in any of the models used.

Finally, when sarcopenia was analyzed as a dependent variable with RLB forward selection based on likelihood ratio, there was no association between covariates + syndrome components (pre-frailty and frailty excluded). However, in the analysis of covariates, prefrailty + frailty (excluding components syndrome) only frailty was associated (OR = 92, 95% CI = 26-322, p = < 0.001).

Discussion

In the literature available to us, we found several studies that have reported the association of vitamin D deficiency and insufficiency and frailty.
However, there is disagreement regarding the criteria to define frailty, as well as the cut-off points for vitamin D, the ages of the adults and, although with significant sample sizes, many of them evaluated predominantly men or women. 7 To the above it is necessary to add that there are very few investigations that have used the Fried criteria and their association with vitamin D insufficiency or deficiency determined by binary logistic regression with the explanatory or predictive model, as was done in ours, with which seemed interesting to divide the individuals according to their vitamin D level into two groups:

– Individuals with figures < 30 ng/mL.
– Individuals with figures < 20 ng/mL.

In addition, to avoid collinearity in our study, the components of the frailty syndrome were evaluated together with all the covariates, excluding the pre-frailty and frailty variables; later these were added and the components of the frailty syndrome were excluded.
There are few studies that have evaluated frailty with the Fried phenotype using a RLB analysis. Ensrud et al. studied a cohort of 6,307 women >69 years of age, in which they reported a prevalence of frailty of 16.4%.

To determine the association between frailty, they divided vitamin D into four categories: <15 ng/mL versus, 15-19.9 ng/mL, 20-29 ng/mL, and >30 ng/mL. The adjusted odds ratios ranged from 1.0 to 1.4 in the different categories with a mild to moderate association.8 In Germany, in a prospective cohort of 727 adults >65 years of age, frailty was identified in 3.9% and vitamin D levels < 15 ng/mL was associated with pre-frailty (OR = 2.4, 95% CI = 1.1-5.3) and mortality (OR = 3.3, 95% CI = 1.0-10.5); however, no association with frailty was identified.9 In another study conducted in a prospective cohort of women > 65 years, a prevalence of frailty of 39% was found; however, there was no association between the 25th percentile of vitamin D (< 14.2 ng/mL) and frailty (hazard ratio of 1.34, 95% CI = 0.941.9).10

Table 2. Bivariate and multivariate binary logistic regression, introduce method.

Variable	Vitamin D				RMb IC 95 % pb			B	Ex (B)		pm
	I + D (n = 132)		Normal (n = 43)						RMm IC 95 %		
	n	%	n	%							
Sex											
Men	22	16.7	8	18.6	0.8	0.3-2.1	0.7	ÿ0.14	0.8	0.2-2.8	0.8
Women	110	82.9	35	81.4	·	·	·	·	·	·	·
Civil status											
Widowhood	45	34.1	12	27.9	1.3	0.6-2.8	0.4	0.15	1.1	0.4-3.1	0.7
Married	38	28.8	11	25.6	1.1	0.5-2.5	0.6	0.19	1.1	0.4-3.1	0.8
Schooling (years) < 6 6 7-9											
10-12	7	5.3	2	4.7	1.1	0.5-2.7	0.6	0.07	1.0	0.1-7.5	0.9
	61	46.2	15	35.9	1.6	0.7-3.2	0.1	0.35	1.4	0.4-4.2	0.5
	28	21	10	23.3	0.8	0.3-2.0	0.7	ÿ0.16	1.1	0.3-3.8	0.7
	17	12.9	6	14	0.9	0.3-2.4	0.8	0.04	0.9	0.2-3.7	0.9
> 12	19	14.4	10	23.3	0.5	0.2-1.3	0.1	·	·		·
Weight											
Normal	25	18.9	6	14	1.4	0.5-3.7	0.4	·	·	·	·
Overweight	56	42.4	26	60.5	0.4	0.2-0.9	0.03	ÿ0.48	0.6	0.1-1.9	0.4
Obesity	51	38.6	11	25.5	1.8	0.8-3.9	0.1	0.36	1.4	0.3-5.2	0.5
previous hospitalizations	17	12.9	4	9.3	1.4	0.4-4.4	0.5	0.05	1.0	0.2-3.7	0.9
previous fractures	21	15.9	6	14.0	1.1	0.4-3.1	0.7	0.31	1.3	0.4-4.3	0.5
Charlson > 2	11	8.3	3	7	1.3	0.3-4.9	0.6	0.46	1.5	0.1-24.5	0.5
a chronic disease	63	47.7	17	39.5	1.3	0.6-2.8	0.3		0.6	0.3-10.9	0.7
polypharmacy	44	33.4	18	41.9	0.6	0.3-1.4	0.3	·	·		·
Weakness	38	28.8	7	16.3	2.0	0.8-5.0	0.1	0.09	1.1	0.3-3.2	0.8
Slow march	38	15.2	2	4.7	3.6	0.8-16.3	0.7	1.33	3.7	0.5-25.5	0.1
low physical activity	62	47	12	27.9	2.2	1.0-4.8	0.02	0.45	1.5	0.6-3.7	0.3
Weightloss	28	21.2	3	7	3.5	1-12.4	0.03	0.94	2.5	0.4-14.1	0.2
Exhaustion	61	46.2	9	20.9	3.2	1.4-7.3	0.003 0.96		2.6	1.0-6.5	0.03
Pre-frailty*	75	56.8	15	34.8	2.4	1.2-5.0	0.01	1.5	4.5	2.0-10.9	< 0.01
Fragility*	30	22.7	3	6.9	3.9	1.1-13.5	0.02	2.2	9.8	2.2-42.6 < 0.01	
Sarcopenia	26	19.7	2	4.7	5	1.1-22.1	0.01	0.22	1.2	0.1-12.1	0.8

R&D: insufficiency+deficiency; bRM: bivariate odds ratio; bp: bivariate; mOR: multivariate odds ratio; pm: multivariate.
*Values excluding fragility components.

In our study, 52% of the adults presented pre-frailty and 18%, frailty; in the multivariate logistic regression analysis, pre-frailty presented a 4.6-fold risk of vitamin D deficiency and a 9.2-fold risk of frailty. The difference with what has been reported by other authors is related to the methodological design, types of covariates, patient ages, cut-off points, ethnic groups or races and, perhaps, also to what we consider vitamin D as a dependent variable in two cut points, while some authors consider frailty phenotypes as dependent variables. Regarding the components of the frailty syndrome, it has been found that weight loss, weakness and exhaustion have been associated with low levels of vitamin D.[8,11] In the bivariate analysis we found that weight loss, weakness , exhaustion and low physical activity were associated with vitamin D levels <30 ng/mL. In the multivariate analysis, only burnout remained associated (OR = 3.2,

95% CI = 1.4-7.3, p = 0.003), an association that did not occur in individuals with vitamin D deficiency. On the other hand, vitamin D has been associated with sarcopenia, falls, fractures, osteoporosis, and loss of vision. independence and is closely related to frailty.12 In this study, sarcopenia occurred in 16% of older adults and was only associated with the frailty phenotype. Finally, polypharmacy and the Charlson comorbidity index were not associated with vitamin D deficiency or sarcopenia.

Conclution

The findings of this study allow frailty to be associated with vitamin D insufficiency/deficiency and sarcopenia.

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Conflicts of interest

The authors declare no conflict of interest.

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ethical responsibilities

Protection of people and animals. The authors declare that no experiments were performed on humans or animals for this research.

Data confidentiality. The authors

They declare that they have followed the protocols of their work center regarding the publication of patient data.

Right to privacy and informed consent. The authors obtained the informed consent

of the patients or subjects referred to in the article. This document is in the possession of the corresponding author.

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