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Association of hypovitaminosis D with triceps brachii muscle fatigability among older women: Findings from the EPIDOS cohort

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ABSTRACT

Background: Vitamin D affects physical performance in older adults. Its effects on muscles, notably on muscle strength, remain unclear. The objective of this cross-sectional study was to determine whether hypovitaminosis D is associated with triceps brachii muscle fatigability in community-dwelling older women.

Methods: A randomized subset of 744 women aged ≥75years from the EPIDOS cohort was categorized into two groups according to triceps brachii muscle fatigability, defined as loss of strength > 5% between two consecutive maximal isometric voluntary contractions. Hypovitaminosis D was defined using consensual threshold values (i.e., serum 25-hydroxyvitamin D concentration [25OHD] ≤10 ng/mL, ≤20 ng/mL, and ≤30 ng/mL). Age, body mass index, comorbidities, use psychoactive drugs, physical activity, first triceps strength measure, hyperparathyroidism, serum concentrations of calcium, albumin and creatinine, season and study centers were used as potential confounders.

Results: The prevalence of hypovitaminosis D ≤ 30 ng/mL was greater among women with muscle fatigability compared with the others (P = .009). There was no between-group difference using the other definitions of hypovitaminosis D. The serum 25OHD concentration was inversely associated with the between-test change in triceps strength (adjusted β = −0.09 N, P = .04). Hypovitaminosis D ≤ 30 ng/mL was positively associated with triceps fatigability (adjusted OR = 3.15, P = .02).

Conclusions: Vitamin D concentration was inversely associated with the ability to maintain strength over time in this cohort of community-dwelling older women. This is a relevant new orientation of research toward understanding the involvement of vitamin D in muscle function.

1. Introduction

Lower concentrations of 25-hydroxyvitamin D (25OHD) are very common in elderly population living in institutions or in the community, reaching up to 90% of older adults [1]. The clinical relevance is that hypovitaminosis D is accompanied by adverse health events. For instance, hypovitaminosis D is associated with poorer physical performance in older adults [2,3]. The explanation most commonly offered is based on the possible involvement of vitamin D in muscle health and function [3], as suggested by experimentation reporting the presence of vitamin D receptors (VDRs) in muscle cells [4]. However, it is noticeable that previous clinical studies on hypovitaminosis D and muscle strength have shown conflicting results [5]. Some cross-sectional studies reported decreased muscle strength in the case of

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hypovitaminosis D [6,7], although others did not find any significant association [8,9]. Moreover, a meta-analysis of interventional trials showed that vitamin D supplementation could not enhance muscle strength after 9 months of supplementation on average [5]. The latter result weakened the plausibility of a link between vitamin D and muscle strength, and strengthened the assumption that vitamin D may impact muscles in a different way.

Muscle strength is inversely related to fatigue [10]. Mechanistically, while the strength depends on the mass of striated muscles, the fatigability (i.e., the muscle ability to continue effort and maintain constant work over time) depends mainly on muscle mitochondrial function. Mitochondrial cofactors enhance the synthesis of ATP, act as a powerful anti-radical, and reduce the level of lactic acid thereby decreasing muscle fatigue [11]. Interestingly, recent findings suggest that vitamin D is involved in mitochondrial oxidative function in skeletal muscles [12]. Specifically, Sinha et al. reported that the energy production during the recovery phase of modest exercise by muscle mitochondria is impaired among people with hypovitaminosis D [12]. Thus, as mitochondrial oxidative phosphorylation is the primary source of cellular ATP, itself source of energy for the myosin-adenosin system in the striated muscle, the suboptimal mitochondrial function accompanying hypovitaminosis D may lead to greater fatigability [12].

We hypothesized that vitamin D status could influence muscle fatigability in older adults. We had the opportunity to examine the association of serum 25OHD concentration with muscle fatigability in a randomized sample of healthy women aged 75 years and older from the large representative community-based EPIDémiologie de l'OStéoporose (EPIDOS) cohort. The objective of the present cross-sectional analysis was to determine whether hypovitaminosis D was associated with triceps brachii muscle fatigability in older women.

2. Methods

2.1. Participants

We studied 744 older women, a randomized subset of the EPIDOS study, a French observational prospective multicentric national cohort designed to evaluate the risk factors for hip fracture among community-dwelling older women. Sampling and data collection procedures have been described in detail elsewhere [13]. In summary, from 1992 to 1994, 7598 women aged 75 years and older were recruited from electoral lists in five French cities (Amiens, Lyon, Montpellier, Paris and Toulouse). Study participants had a blood test and a full medical examination, which consisted of structured questionnaires, information about chronic diseases and a clinical examination. Sera were stored at −100 °C until analyses were performed in a sample of 752 women. This choice of 752 women was based on our budgetarian's capacity to perform the laboratory measure of serum 25OHD concentration. The randomization process was based on the use of a random-number table that generated in an unpredictable, haphazard sequence of number corresponding to the number of subjects included in the study. From this randomized subset of 752 women, all data were available for 744 women.

2.2. Muscle strength measures

The procedure consisted of the evaluation of the maximal isometric voluntary contraction (MVC) strength of the dominant side triceps brachii muscle with dynamometers. Before testing, participants were allowed to practice the isometric movements to warm up, and a trained evaluator gave standardized verbal instructions regarding the test procedure. Isometric elbow extension was measured as the force applied at the hand, with the participant seated on a chair and her shoulder and elbow resting on a support flexed at 90°. The MVC was recorded in Newton (N) using a statergometer (ADCRO [Association pour le Développement de la Chirurgie Réparatrice et Orthopédique] electronic statergometer; ADCRO, Valenton, France). Two MVC were recorded seconds apart. Verbal encouragement was given each time to obtain the maximal score. Between-test change of triceps strength was defined as the difference between the first test and the second one as follows "First strength measure − Second strength measure". Triceps brachii muscle fatigability was defined as the loss of more than 5% of the muscle strength between the first test and the second one. This prevented considering a low inter-measure variability of ≤5% as muscle fatigability.

2.3. Serum vitamin D assessment

Fasting early morning venous blood was collected from resting participants for the measurement of serum 25OHD concentration, a reliable indicator of vitamin D status [14]. Serum 25OHD concentrations were measured by radioimmunoassay (Incstar Corp., Stillwater, MN). With this method, there is no lipid interference, which is often observed in other non-chromatographic assays of 25OHD. The intra- and interassay precision was 5.2% and 11.3%, respectively (range, 12–50 ng/mL in normal adults aged 20–60 years). Hypovitaminosis D was defined using the three most common definitions in the literature, i.e. ≤10 ng/mL, ≤20 ng/mL, and ≤30 ng/mL [14]. All measurements were performed at the University Hospital of Lyon, France.

2.4. Covariates

The following clinical variables were included as potential confounders in the statistical models: age, body mass index (BMI), number of comorbidities, use psychoactive drugs, regular physical activity, and first triceps strength measure. Hyperparathyroidism, serum concentrations of calcium, albumin and creatinine, and the influence of seasons and study centers were also taken into account in the analysis.

2.4.1. Assessment of clinical covariates

Clinical covariates were obtained from a physical examination and a health status questionnaire to target comorbidities (i.e., hypertension, diabetes, dyslipidemia, coronary heart disease, chronic obstructive pulmonary disease, peripheral vascular disease, cancer, stroke, Parkinson disease and depression). Weight was measured with a beam balance scale, and height with a height gauge. BMI was calculated as weight (kg)/height^2 (m^2). Participation in a physical activity was considered regular if participants had practiced at least one recreational physical activity (i.e., walking, gymnastics, cycling, swimming or gardening) for at least one hour per week for at least the past month. Women were asked to bring all the medication they were regularly taking to the clinical center [13]. Psychoactive drugs were benzodiazepines, antidepressants or neuroleptics.

2.4.2. Assessment of biological covariates

Serum intact parathyroid hormone (iPTH) was measured by immunochemoluminometric assay (Magic Lite, Ciba Corning Diagnostic, Medfield, MA; normal range for adults 20–60 year of age, 11–55 pg/mL). The intra- and interassay precisions were 5.2–6.8 and 5.0–5.5% respectively. Hyperparathyroidism was defined as iPTH concentrations ≥65 pg/mL [15].

Serum concentrations of calcium, albumin, and creatinine were determined using automated standard laboratory methods. Because of the high prevalence of hypoalbuminemia in older adults, serum concentrations of albumin and calcium were used to correct the calcium value: corrected calcium = uncorrected calcium + ([40–albumin] × 0.02).

2.5. Statistical analysis

The participants' characteristics were summarized using means and standard deviations (SD) or frequencies and percentages, as