

## Frailty is Highly Prevalent and Associated with Vitamin D Deficiency in Male Nursing Home Residents.

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Dear Editor,

Frailty is recognized as a state of age-related decreased resistance and increased vulnerability to adverse outcomes.<sup>1-3</sup> An increase in recently conducted research on frailty has added mounting evidence to the literature. However, most of the studies focused on non-institutionalized populations and only limited evidence among nursing home (NH) populations exists. As expected, most of the NH patients are very frail.<sup>4</sup> Another common condition among NH populations is vitamin D deficiency.<sup>5</sup> A number of studies have shown associations of vitamin D deficiency with a wide range of skeletal and non-skeletal medical conditions,<sup>6</sup> all of which may contribute to the development of frailty. This study aimed to investigate the association between frailty and vitamin D status among NH patients, which, to our knowledge, has not been examined.

### METHODS

This is a cross-sectional study performed on all male veterans admitted to a NH in 2011-2012.<sup>5</sup> Patient demographic information collected on NH admission included age, body mass index (BMI), ethnicity, education, smoking, alcohol use, place where patients came from, reason for admission, prevalent chronic diseases, serum total 25-hydroxyvitamin D (25(OH)D) level, vitamin D supplementation use, and Activities of Daily Living (ADL). Frailty was measured by using Frailty Index (FI) constructed from 34 deficits. Frailty was defined as FI $\geq$ 0.25.<sup>7</sup> Vitamin D deficiency was defined as 25(OH)D $<$ 20 ng/mL.<sup>6</sup>

Baseline characteristics were compared between frail and non-frail groups using t-tests and chi-square tests. Univariate and multivariate logistic regression models examined associations between frailty and vitamin D status.

### RESULTS

Of 302 male patients admitted to the NH, those without 25(OH)D measured within seven days of admission, with more than 30% of deficit variables missing, or on vitamin D supplementation were excluded, leaving 152 patients. Mean age was 70.3 years, and the majority of the patients were either White (50.0%) or Asian/Pacific Islander (40.1%). Mean FI was 0.37 ranging 0.04-0.63. Prevalence of frailty was 81.6%. Frail patients were significantly older (71.9 vs. 62.8 years) and more likely to be vitamin D deficient (50.0% vs. 28.6%) with lower 25(OH)D levels (20.8 vs. 24.7 ng/mL). (**Table**)

Univariate logistic regression models showed frailty was significantly associated with vitamin D deficiency (OR=2.50, p=0.04) and lower 25(OH)D (OR=0.96 per 1 ng/mL increase, p=0.05). Multivariate logistic regression models adjusted for age, ethnicity, and education showed both

vitamin D deficiency (OR=4.06 , p=0.01) and lower 25(OH)D (OR=0.95 per 1ng/mL increase, p=0.05) were significantly associated with frailty.

## **DISCUSSION**

There has been plausible evidence that supports physiological pathways through which low vitamin D status increases risk of frailty. Low vitamin D levels are associated with poor physical performance<sup>2,8</sup> and symptoms of depression.<sup>9</sup> Vitamin D has also been found to be involved in inflammatory processes.<sup>10</sup> All of these may contribute to developing and worsening frailty.

Our results should be interpreted with caution. The findings may not be generalizable due to the relatively small cohort consisting of only male veterans. Approximately half of patients were excluded due to vitamin D supplement use (n=109, 36.1%) and 25(OH)D not measured within 7 days of admission (n=61, 20.2%). Excluded patients were older (76.4 vs. 70.3 years, p<0.001), had more ADL disabilities (4.0 vs. 3.1, p<0.001), higher FI (0.42 vs. 0.37, p=0.003), and higher BMI (27.3 vs. 25.1, p=0.005). We also lack data regarding sunlight exposure, which may affect serum 25(OH)D levels. Lastly causal relationship cannot be inferred because of the cross-sectional study design.

However, this study has many strengths. First, this is the first study to report on the associations between frailty and vitamin D among NH patients. Second, this study is especially valuable in that the data were collected at the time of NH admission, not at a certain point during NH stay as in most studies. Third, we excluded vitamin D supplement users to reduced bias. The supplement users (n=109) were significantly older (mean age=77.9 vs. 70.3 years old, p<0.001) and frailer (mean Frailty Index=0.42 vs. 0.37, p=0.003), but had higher mean 25(OH)D level (27.1 ng/mL vs. 21.5 ng/mL, p<0.001). This suggests older frailer NH patients may have already been started on supplementation and thus had higher vitamin D levels. Furthermore, the dosage of the supplementation varied greatly from 400 IU daily to as high as 50,000 IU weekly. Vitamin D supplementation would, if not controlled for, significantly confound the results and lead to misinterpretation.

This study showed the prevalence of frailty was high at 81.6%, and lower vitamin D status was significantly associated with frailty among NH patients. Vitamin D supplementation may potentially be an inexpensive and well-tolerated intervention to prevent or reverse frailty.

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## **Author Contributions**

Study concept and design: GK and MT. Acquisition of data: GK. Analysis and interpretation of data: GK and MT. Drafting the article: GK. Revising the article critically for important intellectual content: GK and MT. Final approval of the version to be published: GK and MT.

## **Sponsor's Role**

None

## REFERENCES

1. Clegg A, Young J, Iliffe S, et al. Frailty in elderly people. *Lancet* 2013;381:752-762.
2. Kojima G. Frailty as a Predictor of Future Falls Among Community-Dwelling Older People: A Systematic Review and Meta-Analysis. *J Am Med Dir Assoc* 2015;16:1027-1033.
3. Kojima G. Frailty as a predictor of hospitalisation among community-dwelling older people: a systematic review and meta-analysis. *J Epidemiol Community Health* 2016;70:722-729.
4. Kojima G. Prevalence of Frailty in Nursing Homes: A Systematic Review and Meta-Analysis. *J Am Med Dir Assoc* 2015;16:940-945.
5. Kojima G, Tamai A, Masaki K, et al. Prevalence of vitamin D deficiency and association with functional status in newly admitted male veteran nursing home residents. *J Am Geriatr Soc* 2013;61:1953-1957.
6. Holick MF. Vitamin D deficiency. *N Engl J Med* 2007;357:266-281.
7. Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. *J Gerontol A Biol Sci Med Sci* 2007;62:738-743.
8. Girgis CM, Clifton-Bligh RJ, Turner N, et al. Effects of vitamin D in skeletal muscle: falls, strength, athletic performance and insulin sensitivity. *Clin Endocrinol (Oxf)* 2014;80:169-181.
9. Barnard K, Colon-Emeric C. Extraskeletal effects of vitamin D in older adults: cardiovascular disease, mortality, mood, and cognition. *Am J Geriatr Pharmacother* 2010;8:4-33.
10. Wobke TK, Sorg BL, Steinhilber D. Vitamin D in inflammatory diseases. *Front Physiol* 2014;5:244.

**FIGURE****Table.** Baseline Characteristics of Participants by Frailty Status (N=152)

n (%) or mean $\pm$ SD	Entire Cohort (N=152)	Frailty Status		p-value
		Non-frail (N=28)	Frail (N=124)	
Frailty Index	0.37 $\pm$ 0.14	0.17 $\pm$ 0.04	0.42 $\pm$ 0.11	<0.001
Age (years)	70.3 $\pm$ 12.8	62.8 $\pm$ 8.6	71.9 $\pm$ 13.1	<0.001
Body mass index (kg/m <sup>2</sup> )	27.3 $\pm$ 6.9	26.7 $\pm$ 4.90	27.43 $\pm$ 7.33	0.50
Education (years)	13.0 $\pm$ 2.3	13.3 $\pm$ 2.3	13.0 $\pm$ 2.3	0.50
Ethnicity				
White	76 (50.0%)	18 (64.3%)	58 (46.8%)	0.19
Asian/Pacific islander	61 (40.1%)	9 (32.1%)	52 (41.9%)	
Others	15 (9.9%)	1 (3.6%)	14 (11.3%)	
Reason for admission				
Rehabilitation	60 (39.5%)	11 (39.3%)	49 (39.5%)	-
Skilled-nursing care	42 (27.6%)	17 (60.7%)	25 (20.2%)	
Intermediate care	4 (2.6%)	0 (0.0%)	4 (3.2%)	
Respite	46 (30.3%)	0 (0.0%)	46 (37.1%)	
Place patients came from				
Home	47 (30.9%)	0 (0.0%)	47 (37.9%)	-
Acute care	100 (65.8%)	28 (100.0%)	72 (58.1%)	
other nursing home	5 (3.3%)	0 (0.0%)	5 (4.0%)	
Smoking				
never	53 (34.9%)	10 (35.7%)	43 (34.7%)	0.87
past	71 (46.7%)	12 (42.9%)	59 (47.6%)	
current	28 (18.4%)	6 (21.4%)	22 (17.7%)	
Alcohol				
never	61 (40.1%)	11 (39.3%)	50 (40.3%)	0.88
past	53 (34.9%)	9 (32.1%)	44 (35.5%)	
current	38 (25.0%)	8 (28.6%)	30 (24.2%)	
25(OH)D (ng/mL)	21.5 $\pm$ 9.6	24.7 $\pm$ 8.4	20.8 $\pm$ 9.7	0.05
Vitamin D deficiency	70 (46.1%)	8 (28.6%)	62 (50.0%)	0.04

T-tests used for continuous variables, chi-square tests used for categorical variables.