Osteoporosis International (2021) 32:2217–2224
https://doi.org/10.1007/s00198-021-05970-y

ORIGINAL ARTICLE

Preoperative severe vitamin D deficiency is a significant independent risk factor for poorer functional outcome and quality of life 6 months after surgery for fragility hip fractures

D.S. Sim [1] · K. Tay [1] · T.S. Howe [1] · S.B.J. Koh [1]

Received: 27 October 2020 / Accepted: 19 April 2021 / Published online: 7 May 2021

Abstract

Summary Hip fractures are common in the elderly, and many patients with hip fractures have low vitamin D levels. This study found that severe vitamin D deficiency is linked to poorer recovery of function and quality of life after hip fracture surgery.

Introduction Vitamin D deficiency is prevalent in hip fracture patients and associated with increased mortality and complications. However, there is limited long-term data on how vitamin D levels affect functional outcomes after hip fracture surgery. The aim of this study is to ascertain the association between vitamin D levels and recovery from hip surgery.

Methods Patients who underwent hip fracture surgery from January 2012 to December 2016 and had vitamin D levels assessed during admission were included. Retrospective analysis was performed on patients' demographic data such as age, gender and clinical parameters such as preoperative vitamin D, haemoglobin levels, Charlson Comorbidity Index (CCI), and type and site of surgery. Patients were divided according to four different vitamin D levels—severe vitamin D deficiency (≤10 ng/mL), mild deficiency (10-20 ng/ml), insufficiency (20-30 ng/ml), and normal (>30ng/ml). Functional outcomes were measured by Harris Hip Score (HHS), Parker Mobility Score (PMS), and individual domains of 36-Item Short Form Health Survey (SF36). Univariate and multivariate analyses were conducted to examine the association between vitamin D deficiency and functional outcome scores.

Results Out of 664 patients identified, 9% had severe vitamin D deficiency and 39% mild deficiency. Patients with severe vitamin D deficiency had significantly poorer baseline and 6-month PMS and SF36 Physical Functioning (PF). In multivariate analysis, severe vitamin D deficiency was associated with lower 6-month PMS and SF36 PF.

Conclusion Preoperative severe vitamin D deficiency is an independent risk factor for poorer recovery of function and quality of life after hip fracture surgery.

Keywords Functional outcome · Hip fracture · Vitamin D

Introduction

Hip fracture is an important primary cause of disability in the elderly, increasing the burden of disease in the population and leading to substantial loss of healthy life-years in elderly people [1]. Hip fracture patients have a high prevalence of vitamin D deficiency which has been associated with osteoporosis, muscle weakness, higher fall, and fracture risk in the elderly population [2, 3]. In patients with hip fractures, vitamin D deficiency has also been associated with increased short-term and long-term mortality [4–8], increased complications [5], and poorer cognitive status [9].

There are controversies in the literature concerning vitamin D, and the definition of optimal vitamin D status is still unclear in the literature [10]. There is also no defined link between vitamin D levels and propensity for other metabolic bone diseases apart from rickets, such as osteoporosis which is a well-established risk factor for hip fracture.

Currently, studies have demonstrated that low vitamin D levels are associated with poorer functional outcomes, but some of these studies only assessed short-term outcomes [11, 12], had population sizes less than two hundred patients [12–14], did not account for pre-fracture baseline function [11], and importantly,

✉ D.S. Sim
davidsimshaoen@gmail.com

[1] Department of Orthopaedic Surgery, Singapore General Hospital, Singapore, Singapore

did not assess patients utilizing previously defined vitamin D thresholds [12, 14, 15]. Evaluating serum vitamin D thresholds through studying the effect of vitamin D on functional outcomes may help define target levels of serum vitamin D to optimize recovery of hip fracture patients.

Aim

The aim of this study is to assess for any association between vitamin D levels on admission, stratified along previously defined vitamin D thresholds, and 6-month functional outcome scores after hip fracture surgery, after adjusting for baseline function and other confounders.

Hypothesis

Our hypothesis is that severe vitamin D deficiency is an independent risk factor for poorer 6-month functional outcome after surgery for hip fractures.

Methods

Patient selection

The medical records of patients who underwent hip fracture surgery in our institution, Singapore General Hospital, from January 2012 to December 2016, and had vitamin D levels assessed during admission, were reviewed.

We excluded patients who had pathological fractures, prior surgeries in involved hips, and those resulting from high energy trauma.

Retrospective analysis was performed on patients' demographic data such as age, gender, and clinical parameters such as preoperative vitamin D and haemoglobin levels measured on admission, co-morbidity burden as assessed by Charlson Comorbidity Index (CCI), and type and site of surgery.

Vitamin D definition

Vitamin D in this paper refers to total serum 25-hydroxycholecalciferol, which is reported elsewhere as 25-hydroxyvitamin D or 25(OH) vitamin D or calcifediol. Vitamin D levels were assessed on admission together with other parameters such as serum calcium for bone health assessment and osteoporosis workup.

According to definitions by the Endocrine Society [2], total serum 25-hydroxycholecalciferol levels between of 20–30 ng/ml is termed as vitamin D insufficiency, and that of below 20 ng/ml is termed as deficiency.

Our study utilized ≤10 ng/ml to define severe deficiency; this measure was used in previous studies [4, 5, 16, 17]. Thus, we defined mild vitamin D deficiency using levels of 10–20ng/ml in this study and previous definitions of vitamin D insufficiency (20–30 ng/ml) and normal vitamin D (>30 ng/ml) were retained.

Anaemia definition

Anaemia was defined according to World Health Organization (WHO) gender-based classification. In men, mild anaemia was defined at haemoglobin 11.0–12.9 g/dL; in women, mild anaemia was defined at haemoglobin 11.0–11.9 g/dL. While for both genders, moderate anaemia was defined at haemoglobin 8.0–10.9g/dL and severe anaemia was defined at haemoglobin < 8.0g/dL

Charlson Comorbidity Index

This study used Charlson Comorbidity Index (CCI) to assess co-morbidity burden in hip fracture patients. The CCI score is based on number of conditions including previous myocardial infarction, stroke, and liver disease that are each assigned different weights, with a higher weight representing more severe morbidity. The summation of the weighted comorbidity scores results in a summary score. For statistical analysis, patients in this study were divided into two groups according to their CCI score, CCI 0–1 and CCI ≥2.

Functional outcomes

Functional outcome was measured by the Harris Hip Score and the Parker Mobility Score, while quality of life was assessed using the various domains of the 36-Item Short Form Health Survey (SF36). Harris Hip Score is an assessment of patients' hip with a maximum score of 100 points. Greater emphasis is placed on function as assessed by activities of daily living, gait (47 points), and pain (44 points), while range of motion (5 points) and absence of deformity (4 points) have less weightage in the Harris Hip Score. Parker Mobility Score measures patients' ambulatory status in different situations—indoors, outdoors, or whilst doing shopping, and scores patients from 0 to 9. The use of SF36, Parker Mobility Score, and Harris Hip Score to evaluate outcomes after hip fracture surgery has been validated in previous recent studies [13, 18]. Assessment was performed by independent third-party trained physiotherapists from our Orthopaedic Diagnostic Centre. These assessments were done at baseline on admission and at follow up at 6 months post-discharge at the outpatient clinic. Assessments were done independent of the study and were routinely done in all hip fracture patients.

The duration of 6 months was chosen in view of previous studies which show that functional recovery after hip fracture may be largely complete in the first 6 months [13] and is sufficient to assess midterm recovery from a hip fracture.

For the SF36, patients are assessed using eight different domains divided into two groups: four physical health domains which include physical functioning (SF36 PF), role limitations as a result of physical health problems (SF36 RP), bodily pain (SF36 BP), and general health (SF36 GH), as well as four mental health domains which include vitality (SF36 VI), social functioning (SF36 SF), role limitations as a result of emotional problems (SF36 RE), and mental health perceptions (SF 36 MH).

Baseline pre-operative Harris Hip Score was unavailable, and Harris Hip Score was only assessed at 6 months, as it is not practical to assess pre-operative deformity and range of motion upon admission, due to acute pain.

Statistical analysis

Analysis was performed to determine any correlation between vitamin D levels, and various demographic and clinical parameters. Spearman correlation was performed between two continuous/ordinal variables to determine any monotonic relationships, while the Mann-Whitney *U* test was used to determine if median vitamin D levels were similar between groups of different demographic or clinical parameters.

Patients were subsequently divided into 4 groups according to the vitamin D levels previously defined. Univariate analysis was performed using one-way ANOVA to determine if there was any difference in baseline and 6-month functional outcome scores among the different vitamin D groups.

Multivariate analysis with general linear model was performed on the respective 6-month scores that demonstrate statistically significant differences in outcome amongst vitamin D groups, in order to ascertain the association between vitamin D and recovery from hip surgery, while accounting for other confounders.

All analyses were conducted using SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY). A $p < 0.05$ is considered statistically significant.

Results

Hospital surgical logs identified 664 patients who underwent surgical treatment of osteoporotic hip fractures with available serum total 25-hydroxyvitamin D level recorded between January 2012 and December 2016. The characteristics of our cohort can be seen in Table 1. This study population had a mean age of 77 years; 29% were male and 71% female. Joint-replacing procedures were performed in 55%, and joint-preserving (fixation) procedures in 45%. Of these 664 patients, 9% had severe vitamin D deficiency (≤10 ng/mL), 39% mild vitamin D deficiency (10–20 ng/ml), 42% vitamin D insufficiency (20–30 ng/ml), and 10% normal vitamin D levels (>30ng/ml). Univariate analysis using one-way ANOVA demonstrated that there was a significant difference in 6-month outcome across vitamin D groups as assessed by Parker Mobility Score (p =.003) and SF36 PF (p=.047) (Table 2). There was no significant difference found among vitamin D groups for the other outcome scores.

In a separate analysis, increasing age was significantly correlated to poorer Parker Mobility Score and SF36 PF at 6 months. Parker Mobility Score and SF36 PF were both inversely associated with increasing age (p<0.001 for both), and thus, an initial multivariate analysis investigating the association between vitamin D level, age, and functional outcomes was performed which demonstrated that there is a significant difference in both 6-month PMS and SF36 PF between patients in severe vitamin D deficiency group and patients in all the other vitamin D groups when corrected only for patient's age (Table 3).

After further multivariate analysis, adjusting also for preoperative anaemia, type of surgery, gender, other co-morbidities, and baseline score, severe vitamin D deficiency was found to be an independent risk factor for lower 6-month Parker Mobility Score and SF36 PF(Table 4). Severe vitamin D deficiency was still found to be an independent risk factor for lower 6-month Parker Mobility Score and SF36 PF in the multivariate analysis when baseline scores were excluded from the analysis. Preoperative anaemia, age, and baseline score were found to be independent risk factors for poorer Parker Mobility Score and SF36 PF after hip fracture surgery. Additionally, CCI was found to be an independent risk factor for Parker Mobility Score after hip fracture surgery.

Discussion

The prevalence of vitamin D deficiency (<20ng/ml) in our cohort of surgically treated hip fracture is 48%, which is significantly lower than reported rates of vitamin D deficiency in other study populations (77–87%) [4, 5, 7]. We postulate that this could be due to our equatorial climate. Vitamin D supplementation, type of dwelling, and seasonality have been shown to affect vitamin D levels of hip fracture patients [19]. There was no association between serum vitamin D levels and other clinical parameters such as age, comorbidities, anaemia, and gender (Table 5), which is consistent with the literature [20].

Our study found an association between lower vitamin D levels and poorer baseline ambulatory function based on Parker Mobility Score and quality of life in physical functioning (Tables 2 and 3). The latter measure encompasses carrying out activities of daily living such as groceries, bathing, and dressing. In addition, severe vitamin D deficiency (<10ng/ml) was an independent risk factor for lower Parker Mobility Score and SF36 PF at 6 months after hip fracture surgery in this group, even after accounting for the baseline differences above, meaning that the detrimental effect of severe vitamin D is sustained till at least midterm recovery after a hip fracture.

Table 1 Study cohort characteristics

Characteristic	Value
Population size	664
Age, mean ± standard deviation	77 ± 9
Sex, *n* (%)	
Female	495 (75)
Male	278 (25)
Race, *n* (%)	
Chinese	568 (86)
Malay	37 (5)
Indian	45 (7)
Other	14 (2)
Type of surgery, *n* (%)	
Joint-preserving (fixation)	297 (45)
Joint-replacing	367 (55)
Comorbidities, *n* (%)	
Anaemia on admission	622 (64)
Mild	246 (25)
Moderate to severe	376 (39)
Charlson Comorbidity Index	
0–1	360 (54)
≥2	304 (46)
Serum total 25-hydroxyvitamin D level	
Severe deficiency (≤10 ng/mL)	60 (9)
Mild deficiency (10–20 ng/ml)	257 (39)
Insufficiency (20–30 ng/ml)	278 (42)
Normal (>30ng/ml)	347 (10)
Assessment, *n* (%)	
Completed Medical Outcomes Study 36-item Short Form Survey	611 (92)
Completed Parker Mobility Scale	611 (92)
Completed Harris Hip Scale	544 (82)
6-month mortality, *n* (%)	11 (2)

Our findings build upon the findings of previous studies. Pioli found an association between severe vitamin D deficiency and recovery of pre-fall ambulatory status at 6 months [15]. Di Monaco found an association between severe vitamin D deficiency and a poorer Barthel Index score, which assesses independence in activities of daily living (ADL), after discharge from rehabilitation facilities [11]. Other studies by Leboff and Fischer found associations between severe vitamin D deficiency and poorer lower limb strength over 1 year, and this may indirectly affect ambulatory function and quality of life [13, 14].

While the above studies were able to demonstrate an association between vitamin D deficiency and outcomes after hip fracture surgery, most of these studies were only able to demonstrate this association at a single cut-off value around the range of 6–10ng/ml or severe vitamin D deficiency, similar to that found in our study [12–15].

However, the study by Di Monaco was able to demonstrate a difference in outcome between mild vitamin D deficiency and vitamin D insufficiency, as they used validated vitamin D classes to determine their prognostic capability of the functional recovery after hip fracture [11]. They found that there was a stepwise decrease in ADL when comparing patients with vitamin D insufficiency to those with mild deficiency, and then again between patients who had mild deficiency to those with severe deficiency. There was however no difference in ADL between patients with insufficiency and normal vitamin D levels. Hence, they recommended that patients with vitamin D deficiency should receive supplementation but that there was minimal evidence from their study to increase the threshold for vitamin D supplementation beyond 20ng/ml [11].

We were unable to demonstrate such a difference in outcome between patients with mild vitamin D deficiency and

Table 2 Analysis of 6-month and baseline Parker Mobility Score, Harris Hip Score, and 36-Item Short Form Health Survey (SF36) physical functioning (SF36 PF), role limitations as a result of physical health problems (SF36 RP), bodily pain (SF36) general health (SF36 GH) vitality (SF36 VI), social functioning (SF36 SF), role limitations as a result of emotional problems (SF36 RE), and mental health perceptions (SF 36 MH) score according to vitamin D groups using one-way ANOVA test

		6 months			Baseline		
Variable		Mean	Std. deviation	One-way ANOVA p-value	Mean	Std. deviation	One-way ANOVA *p*-value
Parker Mobility Score	Normal	4.15	2.841	.003	6.26	2.842	.002
	Insufficiency	4.63	2.650		6.67	2.555	
	Deficient	4.50	2.583		6.47	2.609	
	Severe deficiency	3.17	2.307		5.27	2.510	
	Total	4.41	2.642		6.42	2.625	
Harris Hip Score	Normal	72.96	17.155	.181	Not available		
	Insufficiency	75.70	14.394				
	Deficient	76.01	14.734				
	Severe deficiency	71.59	14.616				
	Total	75.19	14.881				
SF36 PF	Normal	35.63	33.040	.047	51.23	30.370	.014
	Insufficiency	35.95	29.214		54.48	30.731	
	Deficient	35.67	28.362		52.76	30.378	
	Severe deficiency	23.73	27.474		40.33	32.402	
	Total	34.79	29.289		52.20	30.888	
SF36 RP	Normal	43.75	44.766	.068	68.12	41.321	.334
	Insufficiency	42.80	44.047		64.39	43.325	
	Deficient	40.38	44.160		62.06	44.144	
	Severe deficiency	25.48	39.757		55.00	42.386	
	Total	40.48	43.973		63.03	43.374	
SF36 BP	Normal	69.19	28.545	.645	74.39	26.645	.472
	Insufficiency	71.30	28.544		79.16	26.816	
	Deficient	73.33	27.164		79.96	25.857	
	Severe deficiency	69.54	29.957		77.95	26.887	
	Total	71.72	28.105		78.86	26.427	
SF36 GH	Normal	68.05	21.537	.096	68.01	21.851	.900
	Insufficiency	67.68	21.811		67.74	21.898	
	Deficient	71.26	19.122		68.32	21.931	
	Severe deficiency	73.92	20.202		65.93	22.591	
	Total	69.64	20.691		67.83	21.929	
SF36 VI	Normal	70.00	23.821	.076	71.23	20.444	.331
	Insufficiency	70.18	23.265		72.84	20.278	
	Deficient	75.08	20.717		74.44	20.343	
	Severe deficiency	71.35	20.583		69.58	23.020	
	Total	72.18	22.210		73.00	20.587	
SF36 SF	Normal	74.80	37.568	.204	86.41	29.162	.160
	Insufficiency	63.76	39.807		85.78	28.715	
	Deficient	63.75	41.256		84.18	30.995	
	Severe deficiency	61.54	41.341		76.23	37.243	
	Total	64.72	40.340		84.36	30.551	
SF36 RE	Normal	88.02	31.085	.128	92.74	24.202	.115
	Insufficiency	95.16	21.093		95.92	19.409	
	Deficient	94.98	21.883		98.18	13.056	
	Severe deficiency	95.52	19.825		97.22	15.417	
	Total	94.37	22.591		96.58	17.527	
SF36 MH	Normal	79.56	19.714	.138	82.67	14.563	.454
	Insufficiency	81.10	18.923		82.58	15.623	
	Deficient	84.15	16.161		83.13	15.980	
	Severe deficiency	80.62	18.835		79.47	17.310	
	Total	82.09	18.010		82.52	15.811	

vitamin D insufficiency. This may be due to the fact that their outcomes were assessed at discharge from rehabilitation facility, whilst ours were assessed at 6 months post-operatively. Their study also utilized a different set of validated outcome scores from this study.

In patients who sustain hip fractures, the majority of which require surgical intervention, Vitamin D deficiency is related to increased complications including pneumonia [5], thromboembolic events [5], and poorer cognitive status [9] which affects rehabilitation after hip fracture surgery. Baseline

Table 3 Age-adjusted multivariate analysis examining association between preoperative serum total 25-hydroxyvitamin D and 6-month Parker Mobility Score and Medical Outcomes Study 36-Item Short Form Survey (SF36) Physical Functioning domain after hip fracture surgery

	Regression estimate (95% confidence interval) *p*-value			
	Parker Mobility Score		SF36 Physical Functioning	
Preoperative serum total 25-hydroxyvitamin D (severe vitamin D deficiency as reference)				
Normal vitamin D	1.05 (0.16 to 1.94)	.021	12.85 (2.72 to 22.97)	.013
Vitamin D insufficiency	1.25 (0.52 to 1.98)	.001	10.07 (1.78 to 18.35)	.017
Vitamin D mild deficiency	1.15 (0.42 to 1.89)	.002	10.23 (−1.90 to 18.56)	.016
Age	−0.10 (−0.12 to −0.08)	<.002	−1.06 (−1.30 to -0.83)	<.001

vitamin D function may also affect recovery after hip fracture through its skeletal and extra-skeletal effects. Vitamin D deficiency is linked to reduced muscle strength and function [3], increased fracture comminution and hence slower recovery [20], impaired bone formation in patients with hip fracture [21], and altered bone turnover markers which are surrogate measures of fracture healing [22]. Our study consolidates the point that pre- and post-hip fracture quality of life is affected by severe Vitamin D deficiency, largely in the domains of physical functioning, consistent with the known effects of Vitamin D on the musculoskeletal system. This is especially important as we strive to develop a healthy and active aging population who may remain socioeconomically viable well into their senior years.

Hence, understanding the association between low vitamin D levels and recovery from hip fracture can help clinicians to identify patients who are at risk for poorer recovery as a target for focused rehabilitation and potentially nutritional supplementation. Further studies are still required to confirm the benefit of vitamin D supplementation in the hip fracture population, many of whom have severe vitamin D deficiency.

Strengths and limitations

This is the study of a large cohort of elderly adults with hip fracture that demonstrates the negative association between severe preoperative serum vitamin D deficiency and midterm functional recovery after hip fracture surgery even after accounting for other confounders. Functional recovery and quality of life were assessed using validated tools. We have a follow-up rate of about 92% of patients who were able to return for assessment at 6 months.

This study however was unable to account for patients who received vitamin D supplementation before their fracture and was also unable to study the effect of vitamin D supplementation after surgical treatment for hip fractures. Our study design was only able to elucidate the association between

Table 4 Results of multivariate analysis examining association between preoperative serum total 25-hydroxyvitamin D and 6-month Parker Mobility Score and Medical Outcomes Study 36-Item Short Form Survey (SF36) Physical Functioning domain after hip fracture surgery

	Regression estimate (95% confidence interval) *p*-value			
	Parker Mobility Score		SF36 Physical Functioning	
Preoperative serum total 25-hydroxyvitamin D (severe vitamin D deficiency as reference)				
Normal vitamin D	0.81 (0.06 to 1.55)	.034	8.75 (0.45 to 17.04)	.039
Vitamin D insufficiency	0.67 (0.05 to 1.28)	.034	3.30 (−3.51 to 10.11)	.342
Vitamin D mild deficiency	0.72 (0.11 to 1.34)	.021	5.02 (−1.81 to 11.86)	.149
Age	−0.06 (−0.07 to −0.04)	<.001	−0.42 (−0.63 to −0.22)	<.001
Charlson Comorbidity Index 0–1 (Charlson Comorbidity Index ≥2 as reference)	0.38 (0.03 to 0.72)	.032	2.88 (0.92 to 6.68)	.137
Preoperative haemoglobin (no anaemia as reference)				
Mild anaemia	−0.21 (−0.63 to 0.22)	.339	−1.31 (−6.00 to 3.39)	.584
Moderate/severe anaemia	−0.62 (−1.01 to −0.22)	.002	−6.10 (−10.46 to −1.74)	.006
Baseline score	0.48 (0.42 to 0.55)	<.001	0.51 (0.44 to 0.57)	<.001
Model adjusted for type of surgery (joint-replacing or joint-preserving/fixation) and gender				

Table 5 Investigation of associations between patient characteristics and vitamin D levels

	Statistical test	Results	
		Spearman's rho correlation coefficient	*p*-value
Age	Spearman's correlation	−0.018	.648
Charlson Comorbidity Index	Spearman's correlation	−0.055	.154
Haemoglobin	Spearman's correlation	0.076	.050
		With vitamin D as continuous variable	
Gender	Mann-Whitney *U*	(with gender as dichotomous variable)	.862
Type of surgery	Mann-Whitney *U*	(with type of surgery as dichotomous variable)	.393

vitamin D at admission and functional recovery, but unable to determine causality.

Conclusion

Prevalence of vitamin D deficiency is high in surgically treated hip fracture patients. Preoperative severe vitamin D deficiency has been shown to be an independent risk factor for slower recovery of function and quality of life after hip fracture surgery. Prospective studies are required to confirm the association between vitamin D and outcomes after hip fracture surgery, to re-define optimal vitamin D levels, and to investigate if vitamin D supplementation can improve recovery in patients with hip fractures.

Code availability Not applicable

Data availability The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate This study involves human data, and institutional review board approval was obtained (Singhealth CIRB 2015/2134) before the start of this single-centre retrospective cohort study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Waiver of consent was approved for this type of retrospective study with anonymized patient records.

Conflicts of interest None.

References

1. Papadimitriou N, Tsilidis KK, Orfanos P, Benetou V, Ntzani EE, Soerjomataram I, Künn-Nelen A, Pettersson-Kymmer U, Eriksson S, Brenner H, Schöttker B, Saum KU, Holleczek B, Grodstein FD, Feskanich D, Orsini N, Wolk A, Bellavia A, Wilsgaard T, Jørgensen L, Boffetta P, Trichopoulos D, Trichopoulou A (2017) Burden of hip fracture using disability-adjusted life-years: a pooled analysis of prospective cohorts in the CHANCES consortium. Lancet Public Health 2:e239–e246
2. Holick MF (2007) Vitamin D deficiency. N Engl J Med 357:266–281
3. Bouillon R, Marcocci C, Carmeliet G, Bikle D, White JH, Dawson-Hughes B, Lips P, Munns CF, Lazaretti-Castro M, Giustina A, Bilezikian J (2019) Skeletal and extraskeletal actions of vitamin d: current evidence and outstanding questions. Endocr Rev 40:1109–1151
4. Lee G-H, Lim J-W, Park Y-G, Ha Y-C (2015) Vitamin D deficiency is highly concomitant but not strong risk factor for mortality in patients aged 50 year and older with hip fracture. J Bone Metab 22:205–209
5. Fakler JKM, Grafe A, Dinger J, Josten C, Aust G (2016) Perioperative risk factors in patients with a femoral neck fracture - influence of 25-hydroxyvitamin D and C-reactive protein on postoperative medical complications and 1-year mortality. BMC Musculoskelet Disord 17:51
6. Nurmi-Lüthje I, Lüthje P, Kaukonen J-P, Kataja M (2015) Positive effects of a sufficient pre-fracture serum vitamin D level on the long-term survival of hip fracture patients in finland: a minimum 11-year follow-up. Drugs Aging 32:477–486
7. Schaller F, Sidelnikov E, Theiler R, Egli A, Staehelin HB, Dick W, Dawson-Hughes B, Grob D, Platz A, Can U, Bischoff-Ferrari HA (2012) Mild to moderate cognitive impairment is a major risk factor for mortality and nursing home admission in the first year after hip fracture. Bone 51:347–352
8. Fisher A, Fisher L, Srikusalanukul W, Smith PN (2018) Usefulness of simple biomarkers at admission as independent indicators and predictors of in-hospital mortality in older hip fracture patients. Injury 49:829–840
9. Carrillo González I, Martínez-Ramírez MJ, Tenorio Jiménez C et al (2020) 25-hydroxyvitamin D levels in the early healing of osteoporotic hip fracture and their relationship with clinical outcome. Nutr Hosp 37(2):327–334. https://doi.org/10.20960/nh.02427
10. Giustina A, Adler RA, Binkley N, Bouillon R, Ebeling PR, Lazaretti-Castro M, Marcocci C, Rizzoli R, Sempos CT, Bilezikian JP (2019) Controversies in vitamin D: summary statement from an international conference. J Clin Endocrinol Metab 104:234–240
11. Di Monaco M, Castiglioni C, Di Carlo S et al (2019) Classes of vitamin D status and functional outcome after hip fracture: a prospective, short-term study of 1350 inpatients. Eur J Phys Rehabil Med 55:56–62
12. Toldy E, Salamon A, Kálmán B et al (2018) Prognostic relevance of circulating 25OHD fractions for early recovery and survival in

patients with hip fracture. J Clin Med Res 7:193. https://doi.org/10.3390/jcm7080193
13. Fischer K, Trombik M, Freystätter G, Egli A, Theiler R, Bischoff-Ferrari HA (2019) Timeline of functional recovery after hip fracture in seniors aged 65 and older: a prospective observational analysis. Osteoporos Int 30:1371–1381
14. LeBoff MS, Hawkes WG, Glowacki J et al (2008) Vitamin D-deficiency and post-fracture changes in lower extremity function and falls in women with hip fractures. Osteoporos Int 19:1283–1290
15. Pioli G, Lauretani F, Pellicciotti F, Pignedoli P, Bendini C, Davoli ML, Martini E, Zagatti A, Giordano A, Nardelli A, Zurlo A, Bianchini D, Sabetta E, Ferrari A, Tedeschi C, Lunardelli ML (2016) Modifiable and non-modifiable risk factors affecting walking recovery after hip fracture. Osteoporos Int 27:2009–2016
16. Bolland MJ, Grey A, Avenell A (2018) Effects of vitamin D supplementation on musculoskeletal health: a systematic review, meta-analysis, and trial sequential analysis. Lancet Diabetes Endocrinol 6:847–858
17. Kennel KA, Drake MT, Hurley DL (2010) Vitamin D deficiency in adults: when to test and how to treat. Mayo Clin Proc 85:752–757 quiz 757–8
18. Sim YE, Sim S-ED, Seng C, Howe TS, Koh SB, Abdullah HR (2018) Preoperative anemia, functional outcomes, and quality of life after hip fracture surgery. J Am Geriatr Soc 66:1524–1531
19. Bischoff-Ferrari HA, Can U, Staehelin HB, Platz A, Henschkowski J, Michel BA, Dawson-Hughes B, Theiler R (2008) Severe vitamin D deficiency in Swiss hip fracture patients. Bone 42:597–602
20. Lakkireddy M, Mudavath SV, Karra ML, Arora AJ (2019) Hypovitaminosis D in patients with osteoporotic hip fractures. J Clin Orthop Trauma 10:768–773
21. Sharma DK, Sawyer RK, Robertson TS et al (2019) Elevated serum 25-hydroxyvitamin D levels are associated with improved bone formation and micro-structural measures in elderly hip fracture patients. J Clin Med Res 8:–1988. https://doi.org/10.3390/jcm8111988
22. Stewart CC, O'Hara NN, Orwig D et al (2019) Serum 25(OH)D is associated with an altered bone turnover marker response after a hip fracture. J Orthop Res 37:535–540