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Vitamin D status and complications, re-admissions, and mortality after hip fracture

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Mini Abstract

Low vitamin D in patients with hip fracture is common. In the present study 407 of 872 (47%) patients had serum calcidiol less than 50 nmol/L. Patients with low vitamin D had more delirium, more new hip fractures and more medical readmissions, but not more orthopaedic complications after 1 year.

Abstract

Purpose: We wanted to study the relation between vitamin D level and postoperative orthopaedic and medical complications in patients with hip fracture. In addition, we investigated the effect of giving a single dose cholecalciferol 100.000 IU. **Methods:** Data were taken from the local Hip fracture register. Logistic regression analyses including vitamin D level and potentially confounding variables were performed for complications and readmissions. **Results:** 407 (47%) of 872 included hip fractures had low vitamin D at baseline. 155 (18%) developed delirium, and the risk was higher in vitamin D deficient patients (Odds Ratio (OR) 1.48 (95% Confidence Interval (CI) 1.04 to 2.12; p=0.03). 261 (30%) were readmitted for non-hip-related conditions. Low vitamin D was associated with a higher risk of medical readmissions within 30 days (OR 1.64 (1.03 to 2.61); p=0.036) and 12 weeks (OR 1.47 (95% CI 1.02 to 2.12); p=0.039). There was a higher risk of a new hip fracture (OR 2.84 (95% CI 1.15 to 7.03) p=0.024) in vitamin D deficient patients. 105 (12%) developed at least one orthopaedic complication, with no correlation to baseline vitamin D. Among vitamin D deficient patients, those receiving a single dose of 100.000 IU cholecalciferol had fewer orthopaedic complications (OR 0.32 (95% CI 0.11 to 0.97) p=0.044) the first 30 days after surgery. **Conclusion:** Low vitamin D at admission for hip fracture increased the risk of delirium, a new hip fracture and medical readmissions, but not orthopaedic complications. The role of vitamin D supplementation to prevent orthopaedic complications requires further study.

Keywords

Hip fracture, vitamin D deficiency, post-fracture complications, fracture healing, delirium, prevention

Declarations

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Introduction

The number of hip fractures is estimated to increase worldwide to 2.6 million by 2025 and 4.5 million in 2050 [1]. Hip fracture rates have declined in Norway the past years [2], but the forecasted ageing of the population might increase the absolute number of fractures [3]. Management of these fractures and change in preventive strategies will remain an important task for healthcare systems globally. Patients with hip fractures are usually elderly, with preexisting comorbidities including cognitive impairment and frequent polypharmacy [4]. Hip fractures are potentially life-changing events that may lead to impaired physical function, loss of independence or death [5]. Acute surgery is almost always required, which increases the risk of surgical and medical complications in an already vulnerable patient [6]. Up to half of the patients may not regain their pre-fracture level of

mobility [7], and every third hip fracture patients require readmission within one year after surgery [4,8]. Improved treatment and secondary prophylaxis may mitigate the adverse effects of hip fractures and reduce associated costs.

Patients with hip fractures have been reported to suffer from low vitamin D [9,10]. Recent studies have identified acute drops in vitamin D level directly after a fracture [11,12]. Adequate vitamin D level is important in maintaining bone health, bone mineralization, and bone resorption, as vitamin D is the key controller of calcium and skeletal homeostasis [13,14]. Low levels of vitamin D may cause secondary hyperparathyroidism leading to high bone turnover followed by bone loss and mineralization defects [15], as well as increased risk of fractures [15,10]. In addition, low levels of 25-hydroxyvitamin D (25(OH)D) have been associated with an increased risk of falls [16,17], adding to an already increased risk of a second hip fracture after an initial hip fracture. Vitamin D supplementation may prevent fractures [18] and has been shown to reduce the risk of falls [19].

There is an ongoing debate regarding optimal doses of vitamin D regimens for supplementation and diagnostic methodology [20]. In addition, the recommended level of circulating 25(OH)D varies from 30 to 100 nmol/L, depending on local recommendations [21]. The influence of vitamin D on bone healing and postoperative complications is not fully understood. Orthopaedic surgeons prescribe vitamin D and calcium to fracture patients to increase the fracture healing process. However, strategies and guidance on fracture healing supplementation are poor, and no human studies have shown clinically relevant increased fracture healing with supplementation of vitamin D. To our knowledge, no studies have found an association between vitamin D levels and postoperative complications after hip fractures. If ensuring an adequate level of vitamin D could reduce the risk of complications and readmissions after a hip fracture, this would be a welcome, and most likely cost-effective, addition to the care.

From May 2014, we routinely measured 25(OH)D in hip fracture patients aiming to improve our secondary fracture prevention. From August 2015, we recommended a loading dose of 100.000 IU cholecalciferol orally for all patients while admitted, in addition to our previous recommendation of 0.5 to 1g calcium and 800 IU vitamin D daily. The main object of this study was 1) To understand the relation between vitamin D deficiency and postoperative orthopaedic complications, especially healing problems. 2) Further we wanted to assess the relation between vitamin D and medical complications and deaths within 1 year. 3) To study adherence to routines on giving cholecalciferol

to hip fracture patients and 4) Evaluate the effect of adding a single dose cholecalciferol 100.000 IU as a standard treatment.

Patients and methods

Patient inclusion and exclusion

All patients admitted with a hip fracture at Oslo University Hospital registered in the local Hip fracture register from May 7th, 2014 to June 9th, 2018 were considered for inclusion in the study.' 1152 fractures in 1122 patients were assessed. Patient inclusion criteria were (i) hip fracture requiring surgery (femoral neck fracture, trochanteric or sub-trochanteric fracture), (ii) available serum 25(OH)D level and (iii) patients resided in the hospital catchment area. Information on deceased patients was obtained from the National Population Register. In 23 cases, a second hip fracture occurred within 1 year, and this was considered to be related to the preceding fracture. In these cases, only the first fracture was included. A second hip fracture occurring after 1 year was included in the study as a separate event (n=7). This left a total of 872 fractures in 865 patients for analysis (Figure 1).

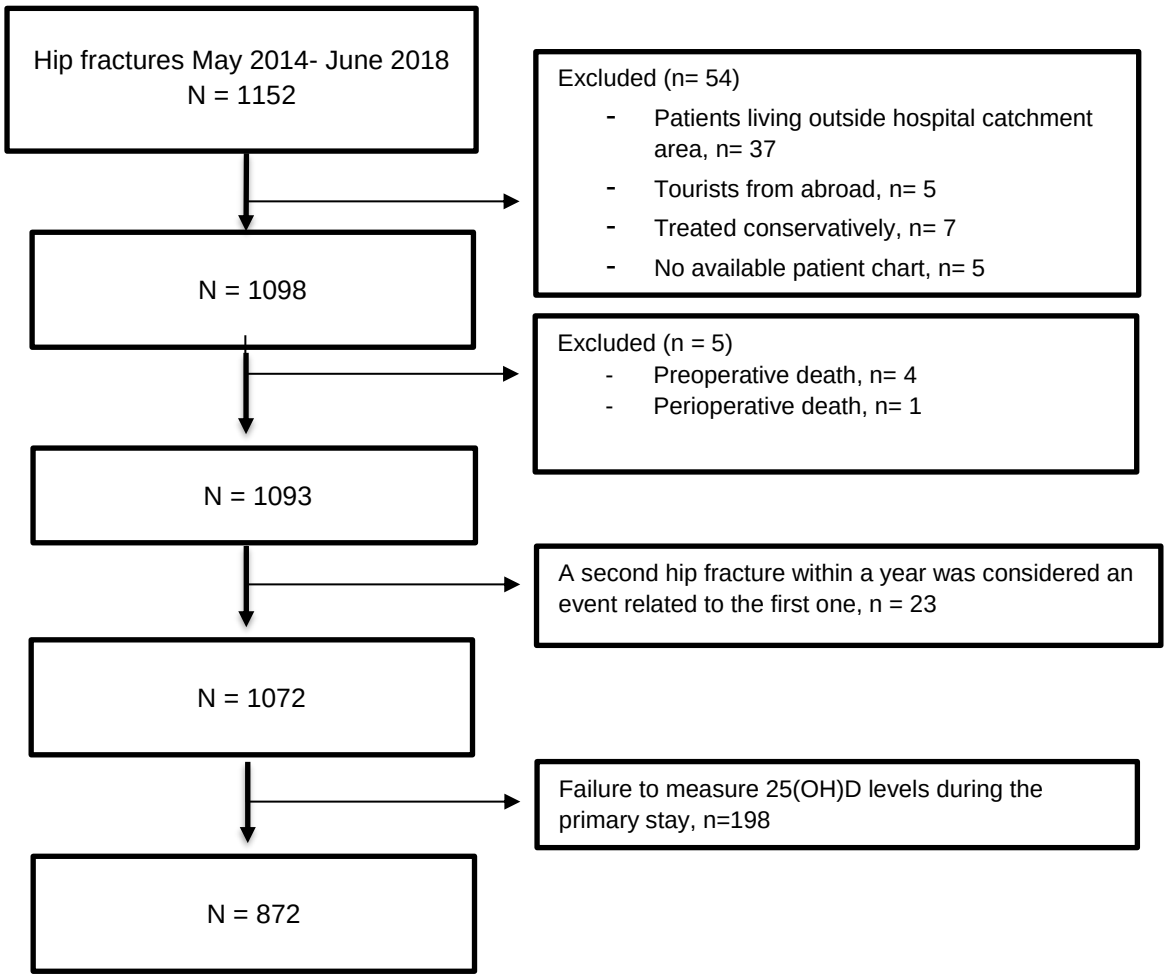

Figure 1. Flow chart of hip fractures included/excluded in the study

Definitions

Vitamin D was quantified by liquid chromatography–tandem mass spectrometry with determination of 25 hydroxyvitamin D2 (25(OH)D2) and 25 hydroxyvitamin D3 (25(OH)D3) levels (Hormone Laboratory, Oslo University Hospital, Oslo, Norway) [22]. The combined concentration of 25(OH)D2 and 25(OH)D3 was considered the patients' 25(OH)D. Blood was drawn the first or second postoperative day. Vitamin D deficiency was defined as serum 25(OH)D level less than 50 nmol/L. Orthopaedic complications were defined as complications related to the hip fracture and initial surgery within 1 year, including surgical site infection, hematoma/bleeding, Trendelenburg gait, peroneal nerve palsy, avascular necrosis, hip instability, mechanical failure of internal fixation, peri-implant-fracture and nonunion. A medical complication was defined as any medical event including infection, renal, respiratory, cardiovascular, gastrointestinal, musculoskeletal or neurological event, that required hospitalization within 1 year after the hip fracture.

Statistical analysis

Continuous data were presented with means and standard deviations (SD), and categorical data were presented as frequencies and proportions. Bivariate analyses were done with Students t-test or chi-square test. Logistic regression analyses were performed on variables from the bivariate analyses with a p-value <0.1. This regression analyses were done to adjust for potentially confounding variables. ASA class, gender, age and pre-fracture level of care were chosen a priori as covariates as they were believed to potentially influence the outcome. In addition, when looking for an effect of the cholecalciferol loading dose we also added osteoporosis treatment as a co-variate to reduce the risk of a false positive finding due to selection bias. The outcome variables of both sets of regression analyses were incidence of complications, readmissions and deaths. We estimated the Variance Inflation Factor (VIF) to detect multicollinearity of the independent variables. Significance was set at $p<0.05$. Statistical analysis was performed using SPSS for Windows version 26 (SPSS Inc, Chicago, IL).

Results

Baseline characteristics

Mean age was 81 years (range 40 to104, SD 11.5). 571 (66%) were female and 322 (37%) were in ASA group 1 or 2 (Table 1). Mean vitamin D level was 52 (range 12 to 134, SD 21.4). With

50 nmol/L as a threshold for deficiency, 407 (47%) were vitamin D deficient and 88 (10%) of them had vitamin D level below 25 nmol/L, indicating severe vitamin D deficiency.

247 (28%) patients developed one or more medical complications during the initial stay (Table 2). The most common were acute post-hemorrhagic anemia 143 (16%), urinary tract infection 129 (15%) and pneumonia 76 (9%). In addition, 155 (18%) were registered with delirium, 84 (21%) in the deficient group and 71 (15%) in the non-deficient group. The risk of delirium was higher in vitamin D deficient patients (OR 1.48 (95% CI 1.04 to 2.12; p=0.03). 33 (4%) developed deep venous thrombosis (DVT) or pulmonary embolism while admitted or within 1 year after discharge, with 21 (5%) in the vitamin D deficient group and 12 (3%) in the non-deficient group (OR 2.07 (95% CI 1.0 to 4.3); p=0.05).

Table 1. Hip fracture patient baseline characteristics regarding vitamin D status measured during hospitalisation

	The whole population (n=872)	**Vitamin D deficient (<50 nmol/L) (n=407)**	**Not vitamin D deficient (>=50 nmol/L) (n=465)**	***p*-value**
Age, mean (SD)	80.5 (11.5)	79.8 (12)	81.2 (11)	0.062
Female, n (%)	571 (66%)	254 (62%)	317 (68%)	0.074
ASA 1-2, n (%)	322 (37%)	148 (36%)	174 (37%)	0.747
Number of hospital days, mean (SD)	6.3 (2.5)	6.3 (2.7)	6.2 (2.4)	0.380
Fracture type, n (%)				0.963
Femoral neck fracture	511 (59%)	239 (59%)	272 (59%)	
Basocervical and trochanteric fracture	325 (37%)	152 (37%)	173 (37%)	
Subtrochanteric fracture	36 (4%)	16 (4%)	20 (4%)	
Surgery within 24 h, n (%)	458 (53%)	205 (50%)	253 (54%)	0.219
Surgery within 48 h, n (%)	758 (87%)	353 (87%)	405 (87%)	0.399
Anti-osteoporotic supplementation during stay, n (%)				0.333
Zolendronate	529 (61%)	239 (59%)	290 (62%)	
Denosumab	77 (9%)	36 (9%)	41 (9%)	
Other	4 (1%)	1 (0%)	3 (0%)	
Received 100.000 IU cholecalciferol loading dose while admitted, n (%)	466 (53%)	206 (51%)	260 (56%)	0.118
Recommended daily supplement of vitamin D and calcium after discharge, n (%)	766 (88%)	353 (87%)	413 (89%)	0.277

Vitamin D status and fracture related complications

105 (12%) patients developed one or more orthopaedic complications within the first year after hip fracture. There was no relation between vitamin D deficiency and the risk of an orthopaedic complication (Table 2). Among the patients with orthopaedic complications, 71 (8%) required secondary surgery within 1 year.

Table 2. Acute complications related to vitamin D status during first hospitalisation after hip fracture. Secondary surgery and orthopaedic complications related to vitamin D status within 1 year after hip fracture, n (%).

	The whole population (n=872)	**Vitamin D deficient (<50 nmol/L) (n=407)**	**Not vitamin D deficient (>=50 nmol/L) (n=465)**	***p*-value**
Acute complications				
One or more medical complications while admitted	247 (28%)	119 (29%)	128 (28%)	0.576
Acute post-hemorrhagic anemia	143 (16%)	65 (16%)	78 (17%)	0.749
Urinary tract infection	129 (15%)	61 (15%)	68 (15%)	0.880
Pneumonia	76 (9%)	36 (9%)	40 (9%)	0.899
Acute cardiovascular disease	52 (6%)	27 (7%)	25 (5%)	0.434
Acute kidney disease	20 (2%)	11 (3%)	9 (2%)	0.450
Secondary surgery				
Secondary surgery within 30 days	35 (4%)	14 (3%)	21 (5%)	0.419
Secondary surgery within 12 weeks	52 (6%)	23 (6%)	29 (6%)	0.716
Secondary surgery within 1 year	71 (8%)	31 (8%)	40 (9%)	0.596
Orthopaedic complications				
Orthopaedic complications within 30 days	49 (6%)	23 (6%)	26 (6%)	0.970
Orthopaedic complications within 12 weeks	67 (8%)	33 (8%)	34 (7%)	0.660
Orthopaedic complications within 1 year	105 (12%)	50 (12%)	55 (12%)	0.836
Nonunion or mechanical failure	42 (5%)	20 (5%)	22 (5%)	0.900
Surgical site infection	34 (4%)	15 (4%)	19 (4%)	0.761
Dislocation of arthroplasty	12 (1%)	6 (2%)	6 (1%)	0.816
Peri-implant fracture	9 (1%)	5 (1%)	4 (1%)	0.591

Vitamin D deficiency and risk for readmission to hospital

261 (30%) patients were readmitted for non-hip-related conditions within 1 year (Table 3). Low vitamin D was associated with a higher risk of medical readmissions at 30 days and 12 weeks post-fracture (Table 3). Analyses of separate diagnoses and diagnosis groups revealed no single diagnosis driving this difference. The most common causes of medical readmission were infections (n=118), with pneumonia as the most common (n=62), followed by urinary tract infection (n=53). Gastrointestinal conditions (n=50) were also common. 122 (14%) patients were admitted 2 or more times, up to a maximum of 6 readmissions the first year. A contralateral hip fracture within 1 year was more common in the vitamin D deficient group. 200 (23%) patients died within 1 year after the first hip fracture. There was no statistically significant relation between vitamin D deficiency and mortality (Table 3).

Table 3. Medical complications, new hip fractures and mortality related to vitamin D status within 1 year after hip fracture, n (%)

				Bivariate analysis	Adjusted analysis [a]		
	The whole population (n=872)	**Vitamin D deficient (<50 nmol/L) (n=407)**	**Not vitamin D deficient (>=50 nmol/L) (n=465)**	***p*-value**	***p*-value**	**OR**	**95% CI [b]**
Medical complications							
Medical readmissions within 30 days	84 (10%)	49 (12%)	35 (8%)	0.024	0.036	1.64	1.03 to 2.61
Medical readmissions within 12 weeks	145 (17%)	80 (20%)	65 (14%)	0.025	0.039	1.47	1.02 to 2.12
Medical readmissions within 1 year	261 (30%)	134 (33%)	127 (27%)	0.071	0.088	1.30	0.96 to 1.75
New hip fractures							
Contralateral hip fracture within 1 year	23 (3%)	16 (4%)	7 (2%)	0.026	0.024	2.84	1.15 to 7.03
Mortality							
Died within 30 days	62 (7%)	29 (7%)	33 (7%)	0.987			
Died within 12 weeks	105 (12%)	54 (13%)	51 (11%)	0.298			
Died within 1year	200 (23%)	101 (25%)	99 (21%)	0.217			

[a] adjusted for sex, age, ASA and pre-fracture level of care

[b] 95% confidence interval (CI) of the odds ratio

Vitamin D loading dose

After the change of routines in August 2015, the treatment with cholecalciferol loading dose went from 7 of 244 (3%) to 459 of 628 (73%; p<0.001) (Table 4). The proportion of patients recommended a daily supplement of at least 800 IU vitamin D daily after discharge decreased from 237 (97%) to 541 (86%; p<0.001). At the same time, patients who were evaluated or treated for osteoporosis increased from 145 (60%) to 529 (85%). We investigated a potential effect of the loading dose of cholecalciferol on orthopaedic complications, secondary surgeries, medical readmissions, and mortality, as well as a contralateral hip fracture, analyzing only the vitamin D deficient patients (n=407). There was a statistically significant correlation between early (within 30

days) orthopaedic complications and revision surgeries, and the single dose of cholecalciferol (Table 5).

Table 4. Adherence to treatment strategy with vitamin D and anti-osteoporosis drugs (AOD [a]) before and after change of routines in August 2015, n (%)

	The whole population (n=872)	**Before routine (n=244)**	**After routine (n=628)**
Osteoporosis treatment			
Treated before admission	28 (3%)	2 (1%)	22 (4%)
Zoledronate while admitted	529 (61%)	92 (38%)	437 (70%)
Denosumab while admitted	77 (9%)	37 (15%)	40 (6%)
Started other AOD [a] while admitted	4 (0.5%)	2 (1%)	2 (0.3%)
Referred to osteoporosis outpatient clinic for evaluation	40 (5%)	12 (5%)	28 (5%)
Not started AOD treatment and not referred	194 (22%)	98 (40%)	96 (15%)
Vitamin D treatment			
Received 100.000 IU cholecalciferol loading dose while admitted	466 (53%)	7 (3%)	459 (73%)
Recommended daily supplement of 800 IU vitamin D after discharge	778 (89%)	237 (97%)	541 (86%)

[a] AOD= anti-osteoporosis drugs

Table 5. Mortality and orthopaedic- and medical complications leading to readmissions related to a loading dose of 100 000 IU cholecalciferol within 1 year in vitamin D deficient patients, n (%), (n=407).

			Bivariate analysis	Adjusted analysis [a]		
	Received cholecalciferol loading dose	**Did not receive cholecalciferol loading dose**	***p*-value**	***p*-value**	**OR**	**95% CI [b]**
Mortality						
Dead within 30 days	8 (4%)	21 (10%)	0.010	0.996	1.00	0.32 to 3.08
Dead within 12 weeks	19 (9%)	35 (17%)	0.015	0.863	1.07	0.49 to 2.37
Dead within 1year	36 (18%)	65 (32%)	0.001	0.186	0.67	0.37 to 1.22
Orthopaedic- and medical complications						
Orthopaedic complications within 30 days	6 (3%)	17 (9%)	0.015	0.044	0.32	0.11 to 0.97
Orthopaedic complications within 12 weeks	11 (5%)	22 (11%)	0.038	0.242	0.58	0.24 to 1.44
Orthopaedic complications within 1 year	19 (9%)	31 (15%)	0.057	0.079	0.53	0.26 to 1.08
Secondary surgery within 30 days	4 (2%)	10 (5%)	0.093	0.047	0.27	0.08 to 0.98
Secondary surgery within 12 weeks	7 (3%)	16 (8%)	0.046	0.081	0.40	0.14 to 1.12
Secondary surgery within 1 year	14 (7%)	17 (9%)	0.528	0.389	0.69	0.29 to 1.62
Medical readmissions within 30 days	23 (11%)	26 (13%)	0.583	0.810	0.91	0.41 to 2.03
Medical readmissions within 12 weeks	35 (17%)	45 (22%)	0.171	0.170	0.66	0.36 to 1.20
Medical readmissions within 1 year	65 (32%)	69 (34%)	0.551	0.201	0.72	0.44 to 1.19
Contralateral hip fracture within 1 year	7 (3%)	9 (5%)	0.575	0.337	0.57	0.18 to 1.78

[a] Logistic regression adjusted for sex, age, ASA, pre-fracture level of care and anti-osteoporosis medication. We found no collinearity between the cholecalciferol loading dose and anti-osteoporosis medication (VIF=1.412).

[b] 95% confidence interval (CI) of the odds ratio

Discussion

We found a high rate of complications during admission and after discharge, emphasizing that patients with hip fractures are vulnerable. Our results confirm that hip fracture patients suffer from low levels of vitamin D which may indicate that elderly with hip fractures do not receive necessary vitamin D supplementation to maintain good bone health. However, the effect of vitamin D supplementation and optimal vitamin D doses for fracture prevention is debated. Some studies and meta-analyses have shown a benefit of vitamin D supplementation [18,19] in fracture prevention, but several report no effect of vitamin D alone, regardless of dose [23-25]. High doses of vitamin D have even been reported to increase the risk of falls and fractures [26].

Orthopaedic complications

Contrary to our initial hypothesis, vitamin D deficiency was not a risk factor for delayed healing or other fracture-related complications in our population. Due to the effects of vitamin D on bone, fracture healing complications could be expected in vitamin D deficient patients. The literature lacks comprehensive data, and findings are not conclusive. Similar to our results, Bodendorfer et al. found no correlation between 25(OH)D levels and healing complications or reoperations [27]. Equally, two small case-control studies identified no difference in the prevalence of vitamin D deficiency in patients with a delayed union or non-union compared to normal fracture healing [28,29]. Others have demonstrated several cases of low serum vitamin D in patients with non-union or delayed union compared with normal bone healing [30-32], implying that vitamin D levels may affect nonunion rate. Brinker et al. suggested that there may be an effect of vitamin D deficiency on clinical fracture healing, as 68% of their patients with non-union were vitamin D deficient [31]. In a review, Gorter et al maintained that vitamin D has a role in fracture healing, but that the available data are too inconsistent to conclude [33].

Medical complications

Almost 30 % of our patients had a medical complication while admitted, which is more than the 20% reported by Fakler et al. [34]. Contrary to Fakler et al we found that acute medical complications during the initial stay seemed unrelated to vitamin D status. One of three patients in our material were readmitted due to medical complications within one year. This is consistent with previous findings [4,8]. There was a statistically significant higher risk of medical readmission during the first three months in patients with low levels of 25(OH)D. An association has been

suggested between low 25(OH)D and increased inflammation due to its effect in innate and acquired host defense [35]. Miller et al. suggest that inflammation, measured on serum interleukin-6, may contribute to prolonged rehabilitation after hip fracture [36]. In elderly with comorbidities, fatigue and inactivity after a hip fracture can lead to infection or exacerbation of a preexisting disease which may further explain the correlation.

Other complications

23 (3%) patients sustained a second hip fracture during the first year with a higher risk in the vitamin D deficient group. This finding is in line with previous studies, suggesting that low serum vitamin D is associated with an increased risk of falls [17,16], and subsequent new hip fracture [9,10]. Interestingly, we found that vitamin D deficient patients had a higher risk of delirium during the primary hospital stay. This is consistent with the case-control study of Torbergsen et al., who found that 51% of hip fracture patients had delirium during hospitalization and that concentrations of 25(OH)D were lower in cases compared with controls [37]. The proportion of patients with delirium in our material was low compared to Torbergsen et al. where delirium was a key variable and actively sought [37]. During our study period, patients were not routinely tested for delirium, hence most patients have likely been diagnosed based on a clinical impression with clear symptoms, such as active confusion or agitation. Vitamin D receptors are located in the brain cortex and hippocampus, which are important areas for cognition, neurotransmission and neuroimmune modulation, including anti-inflammatory and antioxidant effects [38]. Neurotransmission, inflammation and chronic stress are factors in the delirium pathophysiology hypothesis, and vitamin D and other antioxidants inhibit inflammation [39]. Therefore, delirium in vitamin D deficient patients may be caused by increased inflammation as a consequence of reduced anti-inflammatory activity caused by low 25(OH)D.

We also found a correlation between low vitamin D and deep vein thrombosis and pulmonary embolism. Reduced vitamin D level has previously been associated with increased risk of venous thromboembolism [40,41]. Koyama et al. suggested that vitamin D3 exerts anticoagulant effects by upregulating thrombomodulin and downregulating tissue factor expression in acute leukemia cells [41]. In addition, Khademvatani et al. found a significantly higher prevalence of patients with deficient 25(OH)D in the DVT group compared to the control group [40]. However, the prospective population-based study of Brodin et al. found no association between normal serum levels of

25(OH)D and decreased future risk of venous thromboembolism [42]. In addition, a large case-control study found that vitamin D supplementation not was associated with a decreased risk of venous thrombosis after extensive statistical adjustments, suggesting a spurious correlation in previous studies [43].

Cholecalciferol loading dose

Adherence to the new routine with a 100 000 IU cholecalciferol loading dose was achieved in three in four patients (Table 4). We consider this a reasonable goal attainment, bearing in mind that some patients probably had contraindications (e.g. serious renal disease) and others declined this treatment. Interestingly, the proportion of patients receiving osteoporosis treatment increased at the same time as the vitamin D loading dose routine were started, even though the routines for osteoporosis treatment remained unchanged. This may reflect that the attention to medical prevention in general increased through the efforts to implement the change in treatment recommendations. We saw no signs of a negative effect of the single cholecalciferol dose. The cholecalciferol loading dose was on the contrary inversely correlated with early orthopaedic complications and early reoperations (Table 5). However, this needs to be interpreted with caution, as low vitamin D was not a risk factor for orthopaedic complications (Table 2), and the confidence intervals were wide. Even though we adjusted for known risk factors, there is a possibility that patients not receiving the single dose of cholecalciferol were a priori at a higher risk of early complications. On the other hand, if there is a true effect of the additional vitamin D, it is reasonable that this effect is most pronounced in the short term, as oral supplementation of a high dose of vitamin D may have its strongest effect between 7 and 30 days after supplementation [44].

Strengths and limitations

This study is descriptive in nature, and no conclusion may be drawn on cause and effect. Especially the analyses on the potential effect of vitamin D supplements must be interpreted with caution. Several of the statistically significant findings have wide confidence intervals. Our study, however, has a large sample size. We have a complete register with a large amount of data on our patients which makes it possible to do comparative analyses. The cholecalciferol loading dose was given at the hospital and the compliance was therefore high. There was no difference in diagnostic methodology since vitamin D levels were measured in the same way by the same laboratory throughout the period.

The main limitation of our study were the retrospective collecting of important outcome data. The baseline data were collected prospectively, but data after discharge, except mortality were collected by chart review. To decrease the risk of losing data, we excluded patients living outside the hospital catchment area. In our health system, the patients belong by home address to one single hospital for acute cases, and if they are travelling and admitted somewhere else they will be referred to the responsible hospital as soon as possible. We cannot ignore the risk that vitamin D deficiency in the present material is merely a marker of morbidity, as suggested in the study of Autier et al. [45]. We did, however, not find no clear evidence of this when examining vitamin D status against ASA grade, age, gender or permanent nursing home residency, nor when examining collinearity. There was also no correlation between vitamin D deficiency and mortality. More detailed baseline data would have been helpful to further examine this, for instance being able to control for BMI. Most patients were recommended continuous supplementation with vitamin D and calcium, but we have no evidence to what extent this was carried out. Almost no repeat measurements of vitamin D were available. Finally, we have performed multiple comparisons, and cannot exclude that the statistically significant findings are by chance.

Conclusion

Low levels of vitamin D were not correlated with orthopaedic complications and mortality, but with the risk of medical readmissions. There was a higher risk of delirium and a new hip fracture in patients with vitamin D deficiency. 3/4 received 100 000 IU cholecalciferol as per routine. There was a correlation between patients receiving the cholecalciferol loading dose and a lower risk of early orthopaedic complications. Patients who received the loading dose did not have lower risk a medical readmissions or other complications. The consequences of low vitamin D levels in hip fracture patients and the effect of vitamin D supplementation needs to be examined further in large prospective or randomized trials.

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