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## Case report

# The importance of vitamin D in treatment of fracture non-union: A case report

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## ABSTRACT

The prevalence of hypovitaminosis D is currently increasing. A wide variety of diseases and complications are associated with low vitamin D serum concentrations, including poor fracture healing and fracture non-union. A healthy 44-y-old man presented himself with pain due to a non-union of a femoral shaft fracture at 4 y after the initial injury. The fracture had been operated upon three times and was adequately fixated in anatomic position. Hypovitaminosis D was diagnosed, and subsequent supplementation resulted in complete union of the fracture with full pain relief. This case illustrates the importance of adequate serum vitamin D levels in fracture healing, in addition to other fracture healing facilitating factors. With the increasing prevalence of hypovitaminosis D and possibly associated fracture-related complications, routine vitamin D determination should become part of clinical workup in cases of fracture non-union.

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## Introduction

Non-union of fractures occurs in about 5–10% of all fractures [1] and can result from various conditions. Known independent risk factors are fracture severity (open fractures or multiple fracture fragments), the need for operative intervention, fracture location, comorbidities, and the use of benzodiazepines, as well as the use of non-steroidal antiinflammatory drugs in combination with opioids, diuretics, and bisphosphonates [2]. The reason for fracture non-union is not always obvious, and is assumed to be multifactorial. Although the role of vitamin D in fracture healing has not been completely elucidated yet, it is well appreciated that vitamin D plays an important role in all phases of fracture healing [3]. Several recent studies present results that confirm the importance of adequate vitamin D serum levels during fracture healing [2,4,5], but none of them are randomized trials. Although serum vitamin D determination is not routinely performed in cases of fracture non-union [3], vitamin D deficiency and supplementation should have the treating physicians' attention.

This case report presents a patient with a femoral shaft non-union and hypovitaminosis D. Spontaneous healing occurred 4 y posttrauma after normalization of vitamin D serum levels. It illustrates the importance of vitamin D determination and adequate

serum vitamin D levels in fracture healing, in addition to other factors facilitating fracture healing.

## Case report

A 44-y-old healthy man of African descent presented himself at the orthopedic trauma surgery outpatient department at the Leiden University Medical Center, with complaints of pain in his left upper leg 4 y after having sustained a midshaft femoral fracture.

*Initial treatment before our assessment/analysis*

The patient sustained a closed midshaft femoral fracture (Fig. 1A) after his leg was caught between two stacker trucks. Open reduction and intramedullary nailing of the fracture were performed on the day of the injury. Due to inability to bear weight and a slight distraction over the fracture, 5-mm dynamization of the nail was performed 3 mo after the initial procedure. This additional procedure had no effect on the patient's complaints of pain nor on the fracture healing (Fig. 1B). The recovery process progressed slowly, and 1.5 y after initial injury and treatment the patient was able to fully bear weight on both legs but continued to have pain. Repeated radiographs showed no consolidation of the medial and posterior cortex of the femoral fracture.

At 2 y after the initial injury, the patient was referred to an orthopedic surgery clinic. A decortication and autologous bone grafting of the medial and posterior part of the fracture was

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**Fig. 1.** Radiography (A) after initial trauma, (B) after dynamization, (C) at first presentation in our clinic, and (D) after vitamin D supplementation.

performed. The nail had been adequately positioned and remained in situ. A further 14 mo later, x rays revealed some callus formation medially and posteriorly, but the complaints of pain persisted (Fig 1C). During this follow-up period, no blood tests determining vitamin D status were performed.

#### Second opinion and treatment

At our outpatient clinic, the patient's history revealed the use of 10 cigarettes/d and five to ten units of alcohol/wk for at least 10 y. A computed tomography scan of his femur (Fig. 2) showed medial and posterior non-union. Our non-union protocol blood tests (Table 1) revealed a  $\gamma$ -glutamyltransferase level of 110 U/L (normal range, 0–55), a parathyroid hormone level of 17.5 pmol/L (normal range, 0.7–8.0), and a 25-hydroxyvitamin D level of 10 nmol/L (normal range, 50–250). The patient was referred to the department of endocrinology for further analysis. The endocrinologist diagnosed hyperparathyroidism, due to vitamin D deficiency and low dietary calcium intake. A bone densitometry scan showed osteopenic bone. There was no underlying illness causing the patient's hypovitaminosis D. Based on the results of the computed

tomography scan in combination with the hyperparathyroidism, vitamin D supplementation was started as treatment of this non-union. Also, the patient was strongly advised to give up smoking and drinking. For 6 wk the patient received weekly injections of 50 000 IU vitamin D, after which oral supplementation with calcium (500 mg/d) and vitamin D (400 IU/d) was started. After 8 mo of vitamin D supplementation, serum levels had normalized (Table 1). At that time, the patient was able to walk and run without complaints, and radiographs revealed complete consolidation of the fracture (Fig. 1D).

#### Discussion

This case report highlights the importance of routine determination of patients' vitamin D status in cases of fracture non-union. Searching the literature for the effect of vitamin D supplementation in cases of fracture non-union, we found only one publication. Duplantier and Waldron describe a case of a 4-y-old boy with non-union of a clavicle fracture in which hypovitaminosis D played a role [4]. In that case, the patient still needed surgery after vitamin D supplementation to achieve union of the fracture. Several



**Fig. 2.** Computed tomography scan of the partial non-union of the midshaft femoral fracture.

**Table 1**  
Results of non-union protocol blood tests

Component	Before supplementation	After supplementation	Normal range
ALAT, U/L	39	42	0–45
Albumin, g/L	46	49	34–48
Alkaline phosphatase, U/L	107	84	0–115
ASAT, U/L	30	30	0–35
Calcium (albumin corrected), mmol/L	2.25	2.32	2.15–2.55
eGFR (CKD-EPI), mL/min/1.73 m <sup>2</sup>	>90	>90	>60
β-CrossLaps, ng/mL	0.567	–	<0.584
Inorganic phosphate, mmol/L	1.25	–	0.90–1.50
γ-glutamyltransferase, U/L	110	124	0–55
Potassium, mmol/L	4.9	4.5	3.6–4.8
Creatinine, μmol/L	70	77	64–104
Sodium, mmol/L	140	141	136–144
25-hydroxyvitamin D, nmol/L	10	60	50–250
P1NP, ng/mL	41	–	<59
Parathyroid hormone, pmol/L	17.5	3.4	0.7–8.0
TSH, mU/L	1.280	1.450	0.300–4.800
Urea, mmol/L	3.6	–	2.5–7.5

ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; eGFR, estimated glomerular filtration rate; P1NP, procollagen type 1 N-terminal propeptide; TSH, thyroid-stimulating hormone

publications have reported on the role of vitamin D (supplementation) in fracture. A recent large cohort study including more than 300 000 patients with fractures shows that a documented vitamin D deficiency is a risk factor for non-union (odds ratio, 1.14; 95% confidence interval, 1.05–1.22), especially in femoral shaft fractures (odds ratio, 2.15; 95% confidence interval, 1.56–2.96) [2]. Hood et al. also report a high prevalence of low vitamin D levels in orthopedic trauma patients [5]. Sprague et al. recently published a systematic review of eight studies on the efficacy of vitamin D supplementation during fracture healing; all eight report positive effects of vitamin D supplementation, but no randomized controlled trials have evaluated the effect of vitamin D supplementation on fracture healing yet [6].

Haines et al. [7] performed a prospective randomized trial in which a total of 100 people with fracture (89% of the sample) had hypovitaminosis D (both groups combined). In the overall study population, the non-union rate was 4%. There was no significant difference in non-union rate with regard to vitamin D deficiency. It is difficult to relate this study to our case, though, because participants in the study received a single dose of vitamin D supplementation. Brinker et al. [8] report on metabolic and endocrine abnormalities in individuals with non-union. Their study does not find a causal link, but it does show that 83% of the participants screened with non-union have an endocrine disorder such as vitamin D insufficiency or deficiency.

Moore et al. [9] describe the risk factors associated with non-union after elective foot and ankle reconstruction; 76% of their endocrine-disease group experienced non-union, versus 26% in the group without ( $P > 0.05$ ). In this study, endocrine disorders are defined as vitamin D insufficiency or deficiency in 14 participants, hypothyroidism in two, and diabetes mellitus in six. Participants with vitamin D deficiency or insufficiency were 8.1 times more likely to experience fracture non-union.

In our case the patient was a man of African descent. Cosman et al. have published in a review that although there is a high prevalence of vitamin D deficiency in black men and women, there is a lower fracture risk, caused by a higher renal sensitivity for parathyroid hormone [10]. In our case the patient's descent is taken in to consideration, but we do not see it as the main factor causing his non-union. The same consideration is given to his nicotine and alcohol use, but was a previously healthy male who sustained a traumatic injury, not influenced by his substance use.

## Conclusion

In both our case and the case series by Brinker et al. [8] a beneficial effect of vitamin D supplementation is suggested in the treatment of non-union in the presence of a vitamin D deficiency. There are, however, no randomized controlled trials proving a causal link between vitamin D deficiency and the occurrence of fracture non-union. Future clinical trials should investigate the effect of vitamin D supplementation in the treatment of non-union. In the meantime, for clinical daily practice, we conclude that although the evidence is still thin vitamin D determination should be done routinely for every fracture patient with signs of delayed or non-union. This will help optimize the fracture-healing environment and prevent surgical overtreatment.

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