

High prevalence of vitamin D deficiency in elderly patients with advanced osteoarthritis scheduled for total knee replacement associated with poorer preoperative functional state

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ABSTRACT

Vitamin D deficiency has been reported previously in patients with osteoarthritis undergoing total hip arthroplasty. We found a high prevalence of vitamin D deficiency in elderly patients with advanced knee osteoarthritis scheduled for total knee replacement and also a significant association with a lower preoperative functional state. A review of the literature is given on vitamin D deficiency in patients with knee osteoarthritis and the association with lower outcome scores after arthroplasty is discussed.

KEYWORDS

Vitamin D – Deficiency – 25-hydroxyvitamin – Osteoarthritis – Knee – Replacement – Arthroplasty

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Vitamin D is an important fat soluble vitamin that regulates calcium metabolism. The plasma 25(OH)D₃ levels are highly dependent on sunlight exposure and dietary intake, and can be influenced by systemic inflammatory responses as well.¹ Vitamin D deficiency has been found in many chronic diseases and studies have shown that it can also be associated with illness severity in critically ill patients.^{2,5} It has been reported in women with osteoarthritis undergoing total hip arthroplasty.⁴ A high percentage of female patients with hip arthritis have been shown to be osteopenic with signs of increased bone turnover.⁵ Furthermore, an association has been found between vitamin D deficiency and lower functional outcome scores after total hip replacement.⁶ The aim of this study was to investigate vitamin D levels in patients with knee osteoarthritis before arthroplasty and the possible effect on postoperative functional outcome.

We report a high prevalence of vitamin D deficiency in a large group of elderly patients with advanced stages of knee osteoarthritis who are scheduled for total knee replacement. A literature review is given on vitamin D deficiency in patients with knee osteoarthritis and the association with lower outcome scores after arthroplasty is discussed.

Methods

Caucasian patients seen in the preadmission clinic before total knee replacement over one year were included in the

study. None of the patients were taking vitamin D supplements. Vitamin D measurements of plasma 25(OH)D₃ and parathyroid hormone levels were performed in all 139 patients. The vitamin D plasma level was measured from their routine blood samples. The iodine-125 radioimmunoassay (DiaSorin, Stillwater, Minnesota, US) was used for measurement. Weight bearing anteroposterior radiography of both knees was performed for all patients. The patients' sex, age and co-morbidity as classified by the ASA (American Society of Anesthesiologists) grade were documented.

The clinical function of the knee was assessed in the preadmission clinic two weeks before surgery and six months afterwards. Functional outcome was evaluated using the Knee Society score (KSS). The KSS is subdivided into a score that rates function of the knee joint itself and a score that rates the patient's ability to walk and climb stairs.⁷

The patients were divided into two groups according to their 25(OH)D₃ levels. The definition of the National Diet and Nutrition Survey was used to differentiate between vitamin D deficiency (<40nmol/l 25(OH)D₃) and sufficient vitamin D levels (>40nmol/l 25(OH)D₃). Both groups were compared with regard to sex, age and ASA grade.

For statistical analysis, the Student's t-test was used to evaluate the difference between mean knee scores in the two groups before and after total knee replacement. All analysis was performed with SPSS® version 13.0 (SPSS, Chicago, IL, US).

Results

Demographically, the mean age in this group of 159 patients was 71.4 years, with a range of 48–88 years. There were 58 male and 81 female patients. The two groups of vitamin D levels were matched for sex, age and ASA grade. On preoperative weight bearing radiography of the knees, the amount of osteoarthritis was graded according to Kellgren and Lawrence.⁸ All patients were classified as having grade 3 osteoarthritis or higher based on the presence of osteophytes, sclerosis, joint space narrowing and bony deformation.

Plasma 25(OH)D3 levels measured in the 159 patients showed a mean vitamin D level of 58.9nmol/l. In 53 patients, a vitamin D deficiency was found with 25(OH)D3 levels of <40nmol/l. In 106 patients, vitamin D levels were sufficient with 25(OH)D3 levels of >40nmol/l. Based on these results, there was a 24% prevalence of vitamin D deficiency in this group of elderly patients with advanced osteoarthritis. In the vitamin D deficient group, there were 14 male and 19 female patients. A secondary hyperparathyroidism was found in all the patients in this group.

The mean preoperative KSS was significantly lower in the vitamin D deficient group than in the vitamin D sufficient group (31.5 vs 37.1, $p=0.047$). The postoperative KSS was only scored in 102 patients (25 patients from the vitamin D deficient group and 79 from the vitamin D sufficient group). The mean postoperative KSS at six months was also lower in the vitamin D deficient group (74.6 vs 80.4) but this difference was not statistically significant ($p=0.075$).

Discussion

The 24% prevalence of vitamin D deficiency found in these patients is similar to the low vitamin D levels (<40nmol/l) found in 15 of 62 patients before hip replacement as published previously.⁶ The present study is the first that also shows a significant relation between vitamin D deficiency and lower preoperative functional status in elderly patients with advanced knee osteoarthritis.

The strengths of this specific study group are the relatively large number of elderly patients and the fact that the indication for knee replacement implies a very advanced stage in the osteoarthritic disease process. A major limitation of the study is that it was not comparative. As all patients were treated surgically, no conservatively treated control group was available with which to compare the results. Other limitations of this study are that although a large homogenous group was studied, no measurements of weight and height were documented so body mass index was not calculated. Furthermore, bone scintigraphy was not routinely performed preoperatively so bone density was not taken into account. Vitamin D intake and sunlight exposure were not documented but patient data were collected over one year to prevent any seasonal bias.

The study population was restricted to a specific ethnic background, namely Caucasian, and the groups were adequately matched demographically otherwise. Regarding the level quoted for vitamin D deficiency, there is no agreed definition and great variability in the literature. Clinical symp-

toms can be seen at 25(OH)D3 levels below 25nmol/l but based on recent publications, we used a level of <40nmol/l as a cut-off point for vitamin D deficiency.⁶

Literature review

There are few publications regarding the relationship between vitamin D and osteoarthritis of the knee. A search on PubMed using the combined terms 'knee osteoarthritis or gonarthrosis' and 'vitamin D or 25-hydroxyvitamin' resulted in ten relevant articles published on these topics. Tauber *et al* reported on a group of 27 patients scheduled for either total knee replacement or high tibial osteotomy in comparison with a group of 15 patients with hip arthritis.⁹ The plasma vitamin D levels in knee arthritis patients were found to be lower than in hip arthritis patients but when the patients with co-morbidities were excluded, this difference was not significant.

McAlindon *et al* published on the relation of vitamin D levels and the progression of knee osteoarthritis in 556 participants in the Framingham study.¹⁰ The vitamin D intake and serum 25(OH)D3 levels were measured, and weight bearing anteroposterior radiography was scored according to Kellgren and Lawrence on follow-up examinations between 1983 and 1995. It was concluded that low intake and low vitamin D levels (<74nmol/l) appeared to be associated with increased risk for progression of osteoarthritis of the knee with an odds ratio of 2.9 for the lower tertile compared with the upper tertile.

Hunter *et al* performed a case-controlled study in 1,644 female Caucasian twin pairs aged 24–79 years and measured assays for bone turnover, as urinary deoxypyridinoline and calcium regulation including parathyroid hormone and 25(OH)D3, and graded knee osteoarthritis radiologically using the Kellgren and Lawrence classification.¹¹ In the group with knee osteophytes, there was evidence of increased bone turnover, increased parathyroid hormone and decreased vitamin D levels compared with the group without osteophyte formation. After adjustment for age, body mass index and relatedness, all differences disappeared except for a significant increase in urinary deoxypyridinoline. They concluded that bone resorption is increased in the presence of osteoarthritis.

Bischoff-Ferrari *et al* described the association of 25(OH)D3 levels and bone mineral density in knee osteoarthritis in a population-based survey of the Framingham study.¹² A group of 228 patients with radiographic knee osteoarthritis was identified and their vitamin D status classified. The average bone mineral density was compared between vitamin D levels using a linear regression model adjusted for sex, age, body mass index, knee pain, activity, cohort and disease severity. A significant positive association was found between serum 25(OH)D3 and body mass index in patients with knee osteoarthritis independent of the other factors.

Felson *et al* analysed 25(OH)D3 levels in patients from two longitudinal cohort studies: the Framingham osteoarthritis study and the Boston osteoarthritis of the knee study.¹³ In 715 patients in the Framingham study, a mean 25(OH)D3 level of 20ng/ml was found at baseline with 20.5% radio-

graphic worsening on weight bearing radiography of knee osteoarthritis on follow-up with a mean interval of nine years. The 277 patients with osteoarthritis in the Boston osteoarthritis knee study had a mean 25(OH)D3 level of 20ng/ml at baseline with 23.6% of knees showing radiographic worsening on fluoroscopy and magnetic resonance imaging at follow-up after 30 months. No significant association of 25(OH)D3 levels with radiographic worsening was found in either of the cohorts and narrow confidence limits in the analyses suggested that the results were based on insufficient power.

Ding *et al* studied serum 25(OH)D3 levels, and assessed sunlight exposure by questionnaires in 880 randomly selected people aged between 51 and 79 years.¹⁴ Knee pain was assessed, and cartilage volume and defects were measured by magnetic resonance imaging. The measurements were repeated in 353 people 2.9 years later. The results showed a mean serum 25(OH)D3 level of 52.8nmol/l at baseline, and a positive association between sunlight exposure and cartilage volume. A serum 25(OH)D3 level of <50nmol/l was associated significantly with increased joint space narrowing in older people, particularly in women and those with radiographic osteoarthritis and knee pain.

Breijawi *et al* investigated preoperative 25(OH)D3 levels as well as bone mineral density of the lumbar spine and femur in 117 patients with a mean age of 68–70 years, of which 68 had a knee replacement and 49 had a hip replacement.¹⁵ In 84.7% of the patients, a serum vitamin D level of lower than 30ng/ml was found. However, the bone mineral density adjusted for age did not differ from the general population. It was concluded that the high prevalence of vitamin D deficiency was independent of the bone mineral density.

Bergink *et al* looked at a sample of 1,248 elderly people (728 women and 520 men) drawn from the Rotterdam prospective population-based cohort study.¹⁶ Vitamin D intake was determined, and bone mineral density and serum 25(OH)D3 levels were measured at baseline as well as after a mean follow-up period of 6.5 years. Progression of knee arthritis was assessed by comparison of weight bearing radiography at baseline and the last follow-up visit. Progression of radiographic knee arthritis occurred in 5.1% of the highest tertile of vitamin D intake against 12.6% of the lowest tertile. Additionally, a significant relation was found between 25(OH)D3 intake and bone mineral density in association with the incidence of osteoarthritis. In case of a lower bone mineral density at the lumbar spine at baseline, an increased incidence of knee osteoarthritis was seen on radiography with decreasing vitamin D intake and serum 25(OH)D3 levels.

Heidari *et al* compared serum 25(OH)D3 enzyme linked immunosorbent assay measurements between 148 patients with knee osteoarthritis and 150 controls with the same mean age of 60 years.¹⁷ After adjusting for age and sex, a significant lower serum 25(OH)D3 level was found in the osteoarthritis patients subgroup aged younger than 60 years.

Reid *et al* examined plasma 25(OH)D3 and C-reactive protein levels in 33 patients who underwent total knee arthroplasty by blood samples taken preoperatively and

postoperatively for 5 days, with a last sample taken after 3 months.¹ A significant decrease in 25(OH)D3 with increased C-reactive protein was seen directly postoperatively and 25(OH)D3 still remained lower at three months. As a result of the decreased 25(OH)D3 levels after an inflammatory response, it was concluded that 25(OH)D3 cannot be measured accurately in patients with an inflammatory insult.

The vitamin D level can be an important factor that influences the preoperative knee function in osteoarthritic patients but it may also affect the postoperative functional outcome after joint replacement. There is only one study that measured 25(OH)D3 levels in 62 consecutive patients before total hip replacement and assessed outcome by Harris hip scores as well.⁶ It concluded that patients with vitamin D deficiency had lower preoperative functional hip scores and were less likely to obtain an excellent outcome from total hip replacement. As it is known already that preoperative function in general is a good predictor of outcome, the relationship between vitamin D levels and postoperative outcome may therefore simply reflect the association already demonstrated between vitamin D deficiency and lesser preoperative functional status.

Although an association has been found between vitamin D levels and knee function, the exact influence of other underlying factors on this relation still remains unclear. Many personal, clinical and psychosocial factors have been shown to influence functional outcome of arthroplasty in other studies as well. These factors include: income, education, body mass index, disease duration, co-morbidities, contralateral joint pain, use of walking aids, depressive symptoms, low social support, working status, work related knee injuries and workers' compensation claim status.¹⁸

In our study, a higher prevalence of vitamin D deficiency was measured in elderly patients with advanced osteoarthritis scheduled for total knee replacement but the difference in functional outcome postoperatively was not found to be statistically significant. As functional scoring by KSS was only documented in 102 of 139 patients, these missing data could be responsible for lack of power to show any significance at all. This study has shown that vitamin D deficiency has a high prevalence in elderly patients before knee arthroplasty and is related to a poorer functional status preoperatively. Vitamin D supplementation may be a very cost effective means of improving functional outcome postoperatively as well but further research is needed with prospective randomised clinical trials.

Conclusions

Our results indicate that there is a high prevalence of vitamin D deficiency in elderly patients with advanced knee osteoarthritis scheduled for knee arthroplasty. The literature review shows that low dietary vitamin D intake and 25(OH)D3 levels are related with increased risk of knee osteoarthritis, and also that an association with progression of radiographic osteoarthritis is found in several studies. Vitamin D supplementation may improve the vitamin D status but the effect on outcome after total knee replacement requires further research.

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