JBM J Bone Metab 2015;22:205-209
http://dx.doi.org/10.11005/jbm.2015.22.4.205
pISSN 2287-6375 eISSN 2287-7029

Original Article

Vitamin D Deficiency Is Highly Concomitant but Not Strong Risk Factor for Mortality in Patients Aged 50 Year and Older with Hip Fracture

Gyeong-Hak Lee[1], Jung-Won Lim[2], Yong-Gum Park[3], Yong-Chan Ha[2]

[1]Department of Orthopaedic Surgery, National Medical Center, Seoul;
[2]Department of Orthopaedic Surgery, Chung-Ang University College of Medicine, Seoul;
[3]Department of Surgery, Chung-Ang University College of Medicine, Seoul, Korea

Corresponding author

Yong-Chan Ha
Department of Orthopaedic Surgery,
Chung-Ang University College of Medicine,
102 Heukseok-ro, Dongjak-gu, Seoul 06973,
Korea
Tel: +82-2-6299-1577
Fax: +82-2-822-1710
E-mail: hayongch@naver.com

Received: November 18, 2015
Revised: November 25, 2015
Accepted: November 25, 2015

No potential conflict of interest relevant to this article was reported.

Background: The purpose of this study was to ascertain the prevalence of vitamin D deficiency and risk factors associated with mortality in patients ≥50-year-of-age with hip fractures. **Methods:** A total of 489 patients ≥50-year-of-age who sustained a hip fracture from January 2010 to October 2014 were followed-up for a minimum of 1 year. Clinical and radiological outcomes were evaluated including prevalence of vitamin D deficiency. Crude mortality rates were calculated, and the effects of different risk factors on mortality were assessed. **Results:** Vitamin D deficiency was present in 76.5% of cases (n=237). The prevalence of vitamin D insufficiency was 12.3%, and only 11.2% of patients had normal vitamin D levels. Accumulated mortality was 11% (54 patients) at 1 year. A univariate analysis showed that vitamin D deficiency (P=0.012), age (P<0.001), BMI (P<0.001), type of management (P< 0.001), American Society of Anesthesiologists (ASA) score (P=0.009), pre-fracture ambulatory status (P<0.001), and osteoporosis (P< 0.001) were associated with mortality. A multivariate analysis performed using a Cox proportional hazards model demonstrated that ASA score (P=0.001) and pre-fracture ambulatory status (P=0.011) were independently associated with mortality after hip fracture. **Conclusions:** We did not find a relationship between serum 25-hydroxy-vitamin D levels and mortality after hip fracture, although we observed a high prevalence of vitamin D deficiency and a significant association with mortality in the univariate analysis.

Key Words: Hip fractures, Mortality, Risk factors, Vitamin D

INTRODUCTION

Several studies in developed countries have reported a decreasing trend in hip fracture incidence.[1-4] However, studies in Korea show that a two-fold increase in the total number of hip fractures, and the incidence rate of hip fracture in women increased steeply during a 10-year study period.[5] Hip fractures in elderly patients are the most serious because of high mortality, loss of independence, lower quality of life, and the high socioeconomic burden.[6,7] Although most risk factors, such as ageing, sex, and medical comorbidities, are inevitable, aging is the most important risk factor for hip fractures; thus, identifying modifiable risk factors is extremely important. Among these modifiable risk factors, vitamin D defi-

ciency is a known modifiable risk factor for hip fracture.[8] A cohort study in Norway reported that patients in the lowest quartile of 25- hydroxy-vitamin D (25-[OH]D) level had a 38% increased risk of hip fracture compared with those in the highest quartile 25-(OH)D level.[9]

According to a multi-national study, Korea has the highest prevalence (92.1%) of vitamin D insufficiency (25-[OH]D<30 ng/mL), followed by Japan (90.4%), Lebanon (84.9%), Turkey (76.7%), UK (74.5%), Germany (68.0%), Mexico (67.1%), and Spain (64.7%).[10] Song et al.[11] determined the prevalence of vitamin D deficiency in an urban Korean population of 8,976 participants (3,587 men and 5,389 women) aged ≥50-year-of-age. They reported 59.7% and 86.5% prevalence rates of vitamin D deficiency (25-[OH]D <20 ng/mL) in men and women, respectively. Therefore, vitamin D deficiency is a general phenomenon in Korean elderly subjects.[11] However, no study has investigated the association between vitamin D deficiency and mortality in patients with hip fractures.

The purpose of this study was to assess the prevalence and relationship between mortality and vitamin D deficiency among hospitalized patients aged ≥50-year-of-age 50 with hip fractures.

METHODS

A total of 489 patients (489 hips) aged ≥50-year-of-age who was diagnosed with a femoral neck or intertrochanteric fracture from January 2010 to December 2014 were include in this study. Of them, 10 patients had a contralateral hip fracture and were excluded.

The follow-up period was a minimum of 12 months after discharge. There were 146 men (146 hips) and 343 women (343 hips). Demographic datas including age at the time of admission, diagnosis, body mass index (BMI), American Society of Anesthesiologist (ASA) score,[12] T-score (osteoporosis, osteopenia, and normal),[13] pre-fracture ambulatory status using Koval's categories,[14] serum 25-(OH)D_3 level, and type of management were obtained by reviewing the medical records (Table 1).

Blood sampling of all patients at the admission date, after fasting for 8 to 12 hr, was performed by experienced laboratory technicians. Detailed information on the 25-(OH)D assay was provided previously.[15] Briefly, of serum 25-(OH)D levels were assayed with a radioimmunoassay (RIA) kit (Siemens Healthcare, Erlangen, Germany).

Table 1. Demographics of patients

Parameters	Findings
Number of patients	489
Age at the time of admission (yr)	76.5 (50 to 101)
Male:Female	146:343
BMI (kg/m^2)	22.0 (13.3 to 36.2)
Mean of 25-hydroxy-vitamin D_3 levels (ng/mL)	15.7 (0.0 to 112.8)
Diagnosis	
Neck fracture	194 (39.7%)
Intertrochanteric fracture	295 (60.3%)
Type of management	
Internal fixation	160 (32.7%)
Arthroplasty	312 (63.8%)
Conservative	17 (3.5%)
ASA score	
1	1 (0.2%)
2	137 (28.0%)
3	346 (70.8%)
4	5 (1.0%)
Osteoporosis	
Normal	19 (3.9%)
Osteopenia	111 (22.7%)
Osteoporosis	359 (73.4%)
Koval's grade by pre-fracture	
I	38
II	20
III	7
IV	14
V	15
VI	7
VII	1

BMI, body mass index; ASA, American Society of Anesthesiologist.

Routine follow-up visits were scheduled at 6 weeks, and 3, 6, 9, 12 months, and every year thereafter. Patients who had not returned for regularly scheduled visits were contacted by telephone.

Osteoporosis was defined as a T-score ≤-2.5, osteopenia was defined as a T-score between -1 and -2.5, and normal was defined as a T-score ≥-1.0.[13]

Activity levels were defined as follows: I-independent community ambulator, II-community ambulator with cane, III-community ambulator with walker/crutches, IV-independent household ambulator, V-household ambulator with cane, VI-household ambulator with walker/crutches, and VII-nonfunctional ambulatory.[14]

According to the Holick [16] classification, vitamin D deficiency was considered at a vitamin D level <20 ng/mL, vitamin D insufficiency was 21 to 29 ng/mL, and normal ≥30 ng/mL. In addition, severe vitamin D deficiency was <10 ng/mL.[17]

http://dx.doi.org/10.11005/jbm.2015.22.4.205

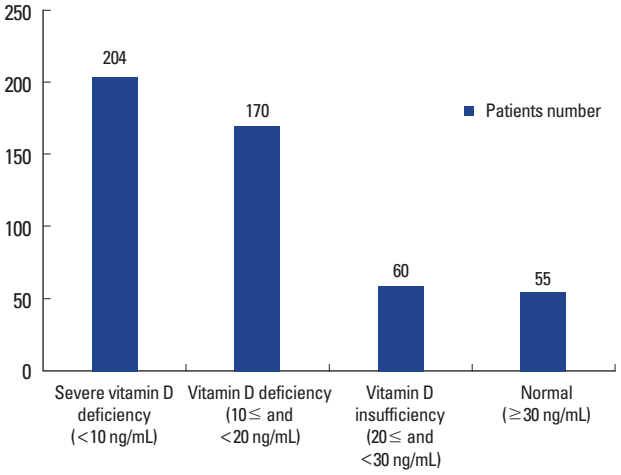

Fig. 1. High prevalence of vitamin D deficiency in patients ≥50-year-of-age with hip fracture.

Mortality was determined by the hospital records and/or by interviewing the patient's family. A systemic search for death certificates at the National Statistical Office was conducted for patients lost to follow-up.

1. Statistical analysis

Sex, age, diagnosis, type of management, BMI, ASA score, T-score (osteoporosis, osteopenia, and normal), pre-fracture ambulatory status, and serum 25-(OH)D_3 levels were assessed to determine their relationships with mortality. We used the chi-square or Fisher's exact tests for categorical variables and the t-test for numerical variables. All two-sided *P*-values<0.05 were considered significant. A multivariate analysis was performed using age, gender, BMI, type of management, ASA, osteoporosis, pre-fracture ambulatory status, and serum 25-(OH)D_3 levels as these variables had *P*-values <0.10. The Cox proportional-hazards model was carried out to identify independent factors associated with mortality. The statistical analysis was performed using SPSS version 20 software (SPSS Inc., Chicago, IL, USA).

RESULTS

The mean vitamin D level at admission was 15.7 ng/mL. The prevalence of vitamin D deficiency was 76.5%, 12.3% of patients were vitamin D insufficient, with 11.2% had normal vitamin D levels. Of them, severe vitamin D deficiency was present in 41.7% (204/489 patients) (Fig. 1).

During the minimum 1-year follow-up period, 114 of 489 patients (23.3%) died. Of them, 54 died within 1 year, 32 within 2 years, 11 within 3 years, and 17 within 5 years.

Table 2. Comparison of parameters regarding mortality in patients with hip fractures

	Survival	Mortality	*P*-value
Number (%)	375 (76.7)	114 (23.3)	
Gender (M/F)	109/266	37/77	0.489
Age (yr) (mean±SD)	74.5±10.1	83.4±7.6	<0.001
BMI (mean±SD)	22.3±3.3	21.0±3.2	<0.001
Diagnosis			0.626
Neck fracture	151	43	
Intertrochanteric fracture	224	71	
Type of management			<0.001
Internal fixation	141	19	
Arthroplasty	224	88	
Conservative	10	7	
ASA score			0.009
1	1	0	
2	117	20	
3	255	91	
4	2	3	
Osteoporosis			<0.001
Normal	97	17	
Osteoporosis	253	122	
Pre-fracture ambulatory status			<0.001
Koval I-III	310	68	
Koval IV-VII	65	46	
Serum Vitamin D level			0.001
Less than 10 ng/mL	138	66	
10 ng/mL to less than 20 ng/mL	144	26	
20 ng/mL to less than 30 ng/mL	50	10	
More than 30 ng/mL	43	12	

SD, standard deviation; BMI, body mass index.

The univariate analysis showed that mortality was associated with vitamin D deficiency (*P*=0.012), age (*P*<0.001), BMI (*P*<0.001), type of management (*P*<0.001), ASA score (*P*=0.009), pre-fracture ambulatory status (*P*<0.001), and osteoporosis (*P*<0.001). However, no significant association was found between mortality and sex (*P*=0.489) or diagnosis (*P*=0.626) (Table 2). The adjusted multivariate analysis revealed that ASA score (HR 12.220; 95% CI 3.314-45.063, *P*=0.001) and pre-fracture ambulatory status (HR 1.681; 95% CI 1.104-2.558, *P*=0.011) were significant associated with death after hip fracture.

DISCUSSION

Our results show a high prevalence of hypovitaminosis D and mortality in patients with hip fracture. In total, 89% of patients were vitamin D deficient or insufficient, and 1-year mortality after hip fracture was 11%. Although vita-

min D deficiency was a possible risk factor for death after hip fracture, we did not find any strong evidence for vitamin D deficiency as risk factor for death after hip fracture. Medical comorbidities and preoperative ambulatory status were important risk factors for mortality after hip fracture in this study.

Although the mean vitamin D insufficiency (<30 ng/mL) rate was 63.9% in a multinational study of 18 countries that evaluated 2,606 postmenopausal women with osteoporosis, South Korea had the highest rate (92.1%) of vitamin D insufficiency (<30 ng/mL) among the 18 countries.[10] Choi [18] evaluated the 2008 Korea National Health and Nutrition Examination Survey IV data that included 6,925 subjects in the general population and reported vitamin D deficiency (<20 ng/mL) prevalence rates of 47.3% in men and 64.5% in women and those for vitamin D insufficiency (<30 ng/mL) were 86.8% in men and 93.3% in women. In this study, vitamin D insufficiency (<30 ng/mL) and deficiency (<20 ng/mL) were present 88.8% and 76.5% of subjects, respectively. The reason for the high vitamin D insufficiency rate in Korea may be due to the indoor lifestyle and protection from ultraviolet light.[18]

The relationship between vitamin D deficiency and mortality in elderly subjects has been reported in several studies.[19-21] However, serum vitamin D concentrations and mortality rates in elderly patients with hip fractures are rarely reported.[22,23] Although our univariate analysis found that vitamin D deficiency was an independent risk factor for mortality after hip fracture, it was not associated with mortality after adjusting for age ($P<0.001$), BMI ($P=0.041$), type of management ($P<0.001$), ASA score ($P=0.009$), pre-fracture ambulatory status ($P<0.001$), and osteoporosis ($P<0.001$) in the multivariate analysis. This finding is similar to a previous study. Gumieiro et al.[22] assessed whether serum vitamin D concentration is associated with gait status and mortality among 87 elderly patients with fractures of the proximal femur 6 months after suffering the fracture. They reported that serum vitamin D concentration was not related to gait status or mortality among patients with fractures proximal femur.[22] Madsen et al.[23] performed a case control study of 562 patients aged ≥70 years with hip fractures and found that serum parathyroid hormone serum calcium levels were significantly associated with mortality, whereas serum 25-(OH)D level was not.

Risk factors for mortality after hip fracture have been reported in several studies.[24-28] The known risk factors for mortality after hip fracture are race, old age, dementia, male sex, low BMI, low handgrip strength, preoperative activity, preoperative delirium, and medical comorbidities, such as chronic renal failure, congestive heart disease, and chronic obstructive pulmonary disease.[6,25-29] In that study, the patient's medical condition according to the ASA score and preoperative functional status by the Koval's classification were important risk factors for mortality after hip fracture. In a previous Jeju cohort study, Lee et al.[6] performed mid-term follow-up after hip fracture in patients >50 year old. After adjustment for covariates, age, woman sex, and medical comorbidities were significantly associated with the risk for mortality after hip fracture.[6] However, preoperative functional activity was not associated with the risk for mortality. Karademir et al.[29] reported no significant association between ASA score and mortality after hip fracture in patients >75-year-old. The reason for these discrepancies might be related to cohort size, sex distribution, and patient age or other demographic characteristics.

This study had several limitations. First, it was a retrospective review of prospectively collected data, and no control group was used. Second, a single blood 25-(OH)D measurement is an imperfect surrogate as a long-term indicator of 25-(OH)D. Finally, serum 25-(OH)D levels were measured at baseline by radioimmunoassay. Therefore, further study is necessary to evaluate the real-time effect of vitamin D.

In conclusion, we did not find a relationship between serum 25-(OH)D level and mortality after hip fracture, although we observed high prevalence of vitamin D deficiency and a significant association with mortality in a univariate analysis.

REFERENCES

1. Cassell E, Clapperton A. A decreasing trend in fall-related hip fracture incidence in Victoria, Australia. Osteoporos Int 2013;24:99-109.
2. Leslie WD, O'Donnell S, Jean S, et al. Trends in hip fracture rates in Canada. JAMA 2009;302:883-9.
3. Adams AL, Shi J, Takayanagi M, et al. Ten-year hip fracture incidence rate trends in a large California population, 1997-2006. Osteoporos Int 2013;24:373-6.
4. Icks A, Haastert B, Wildner M, et al. Trend of hip fracture

http://dx.doi.org/10.11005/jbm.2015.22.4.205

incidence in Germany 1995-2004: a population-based study. Osteoporos Int 2008;19:1139-45.
5. Ha YC, Park YG, Nam KW, et al. Trend in hip fracture incidence and mortality in Korea: a prospective cohort study from 2002 to 2011. J Korean Med Sci 2015;30:483-8.
6. Lee SR, Ha YC, Kang H, et al. Morbidity and mortality in Jeju residents over 50-years of age with hip fracture with mean 6-year follow-up: a prospective cohort study. J Korean Med Sci 2013;28:1089-94.
7. Yi H, Ha YC, Lee YK, et al. National healthcare budget impact analysis of the treatment for osteoporosis and fractures in Korea. J Bone Metab 2013;20:17-23.
8. Autier P, Boniol M, Pizot C, et al. Vitamin D status and ill health: a systematic review. Lancet Diabetes Endocrinol 2014;2:76-89.
9. Holvik K, Ahmed LA, Forsmo S, et al. Low serum levels of 25-hydroxyvitamin D predict hip fracture in the elderly: a NOREPOS study. J Clin Endocrinol Metab 2013;98:3341-50.
10. Lips P, Hosking D, Lippuner K, et al. The prevalence of vitamin D inadequacy amongst women with osteoporosis: an international epidemiological investigation. J Intern Med 2006;260:245-54.
11. Song HR, Kweon SS, Choi JS, et al. High prevalence of vitamin D deficiency in adults aged 50 years and older in Gwangju, Korea: the Dong-gu Study. J Korean Med Sci 2014;29:149-52.
12. White BL, Fisher WD, Laurin CA. Rate of mortality for elderly patients after fracture of the hip in the 1980's. J Bone Joint Surg Am 1987;69:1335-40.
13. WHO Study Group. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ Tech Rep Ser 1994;843:1-129.
14. Koval KJ, Aharonoff GB, Rosenberg AD, et al. Functional outcome after hip fracture. Effect of general versus regional anesthesia. Clin Orthop Relat Res 1998:37-41.
15. Looker AC, Dawson-Hughes B, Calvo MS, et al. Serum 25-hydroxyvitamin D status of adolescents and adults in two seasonal subpopulations from NHANES III. Bone 2002;30:771-7.
16. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:266-81.
17. Bischoff-Ferrari HA, Can U, Staehelin HB, et al. Severe vitamin D deficiency in Swiss hip fracture patients. Bone 2008;42:597-602.
18. Choi HS. Vitamin d status in Korea. Endocrinol Metab (Seoul) 2013;28:12-6.
19. Ginde AA, Scragg R, Schwartz RS, et al. Prospective study of serum 25-hydroxyvitamin D level, cardiovascular disease mortality, and all-cause mortality in older U.S. adults. J Am Geriatr Soc 2009;57:1595-603.
20. Fiscella K, Franks P. Vitamin D, race, and cardiovascular mortality: findings from a national US sample. Ann Fam Med 2010;8:11-8.
21. Wang JB, Abnet CC, Chen W, et al. Association between serum 25(OH) vitamin D, incident liver cancer and chronic liver disease mortality in the Linxian Nutrition Intervention Trials: a nested case-control study. Br J Cancer 2013;109:1997-2004.
22. Gumieiro DN, Pereira GJ, Minicucci MF, et al. Associations of vitamin D deficiency with postoperative gait and mortality among patients with fractures of the proximal femur. Rev Bras Ortop 2015;50:153-8.
23. Madsen CM, Jørgensen HL, Lind B, et al. Secondary hyperparathyroidism and mortality in hip fracture patients compared to a control group from general practice. Injury 2012;43:1052-7.
24. Colais P, Di Martino M, Fusco D, et al. The effect of early surgery after hip fracture on 1-year mortality. BMC Geriatr 2015;15:141.
25. Paksima N, Koval KJ, Aharanoff G, et al. Predictors of mortality after hip fracture: a 10-year prospective study. Bull NYU Hosp Jt Dis 2008;66:111-7.
26. Chatterton BD, Moores TS, Ahmad S, et al. Cause of death and factors associated with early in-hospital mortality after hip fracture. Bone Joint J 2015;97B:246-51.
27. Alegre-López J, Cordero-Guevara J, Alonso-Valdivielso JL, et al. Factors associated with mortality and functional disability after hip fracture: an inception cohort study. Osteoporos Int 2005;16:729-36.
28. Meyer HE, Tverdal A, Falch JA, et al. Factors associated with mortality after hip fracture. Osteoporos Int 2000;11:228-32.
29. Karademir G, Bilgin Y, Erşen A, et al. Hip fractures in patients older than 75 years old: Retrospective analysis for prognostic factors. Int J Surg 2015. http://dx.doi.org/10.1016/j.ijsu.2015.11.009.