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Serum Vitamin D Status as a Predictor of Prognosis in Patients with Acute Ischemic Stroke

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Key Words
Vitamin D · Ischemic stroke · Outcome

Abstract
Background: Low 25-hydroxyvitamin D (25(OH)D) concentrations have been shown to predict risk of cardiovascular disease and all-cause mortality. Although the prevalence of 25(OH)D deficiency is high in patients with acute stroke, the prognostic value of 25(OH)D in stroke has not been clearly established. The purpose of this study was to determine whether the baseline serum 25(OH)D level was associated with the functional outcome in patients with acute ischemic stroke. ***Methods:*** From June 2011 to January 2014, consecutive patients with acute ischemic stroke within 7 days of symptom onset were enrolled in this study from a prospectively maintained stroke registry. Serum 25(OH)D level was measured at admission. Clinical and laboratory data including stroke severity using the National Institute of Health Stroke Scale (NIHSS) score were collected during admission, and the functional outcome at 3 months was assessed by modified Rankin scale (mRS). The association between the baseline 25(OH)D level and a good functional outcome (mRS 0–2) at 3 months was analyzed by multiple logistic regression models. ***Results:*** A total of 818 patients were enrolled in this study. Mean age was 66.2 (±12.9) years, and 40.5% were female. The mean 25(OH)D level was 47.2 ± 31.7 nmol/l, and the majority of patients met vitamin D deficient status (<50 nmol/l; 68.8%), while an optimal vitamin D level (≥75 nmol/l) was present in only 13.6% of the patients, and 436 (53.3%) patients showed good functional outcome at 3 months. Serum 25(OH)D levels in patients with good outcomes were significantly higher than those with poor outcome (50.2 ± 32.7 vs. 43.9 ± 30.0 nmol/l, p = 0.007). The 3-month functional outcome was significantly associated with month-specific 25(OH)D quartiles in multivariable logistic regression analysis. After adjustment for age and sex, the highest 25(OH)D quartile group had higher tendency for good functional outcome at 3 months (odds ratio (OR) = 1.68, 95% confidence interval (CI) = 1.13–2.51). After fully adjusting for other potential confounders, such as stroke severity and vascular risk factors, the association was further strengthened with an OR (95% CI) of 1.90 (1.14–3.16). Other factors associated with good functional outcome in multivariable analysis were younger age, lower initial NIHSS score and absence of diabetes. ***Conclusions:*** This study suggests that serum 25(OH)D level is an independent predictor of functional outcome in patients with acute ischemic stroke. Further studies are required to determine whether vitamin D supplementation could improve functional outcome in patients with ischemic stroke.

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Introduction

Vitamin D deficiency has been implicated as an independent risk factor for cardiovascular outcomes and all-cause mortality in several large prospective studies and meta-analysis [1–7]. Low vitamin D level has also been correlated with risk factors for cardiovascular disease (CVD) such as diabetes and hypertension [8, 9]. Whether this relationship is causal and modifiable by vitamin D supplementation has not yet been determined in a well-powered clinical trial. However, another prospective study cast doubt on the association between vitamin D level and CVD [10], and several other studies have suggested ethnic difference of implication of vitamin D deficiency [11]. The MESA study demonstrated that vitamin D deficiency is associated with incident coronary heart disease in white or Chinese but not in black or Hispanic participants [12]. Recently, a few studies have suggested the association between vitamin D status and functional outcome of acute stroke [13–15]. However, it remains to be determined whether a low vitamin D level is associated with stroke outcome. Therefore, we studied the association between the baseline vitamin D level and the 3-month functional outcome in patients with acute ischemic stroke.

Methods

Study Population

From June 2011 to January 2014, 985 consecutive patients with acute ischemic stroke who visited a single tertiary university hospital within 7 days of symptom onset were initially considered for enrollment in this study from the prospectively maintained stroke registry. Clinical diagnoses were based on brain CT and/or MRI. Among these 985 patients, 68 were excluded due to a premorbid modified Rankin scale (mRS) score of ≥3, and 37 were excluded because their follow-up lacked outcome information. Furthermore, 62 patients were excluded as 25-hydroxyvitamin D (25(OH)D) was not assayed in their blood samples during the acute stage. Therefore, 818 participants were enrolled, and their data were analyzed (fig. 1). Clinical and demographic characteristics, risk factor profiles and data on neurological findings were abstracted from our prospectively maintained stroke registry. The functional outcomes were assessed using the mRS score at 3 months. One of 3 board-certified neurologists (P.-W.C., Y.B.K. and H.-S.M.) measured the mRS score. A poor outcome was defined as a 3-month mRS score of 3–6, and a good outcome was when the mRS score was from 0 to 2.

The protocol for this study was approved by the institutional review board. The board permitted the study to waive informed consent for data collection and analysis because this was a retrospective, registry-based study.

Serum 25(OH)D

25(OH)D was assayed in the morning of the second day within 24 h of admission. Liquid chromatography tandem mass spectrometry was used to determine the serum level of 25(OH)D, and the coefficient of variation was <10%. To adjust for seasonal varia-

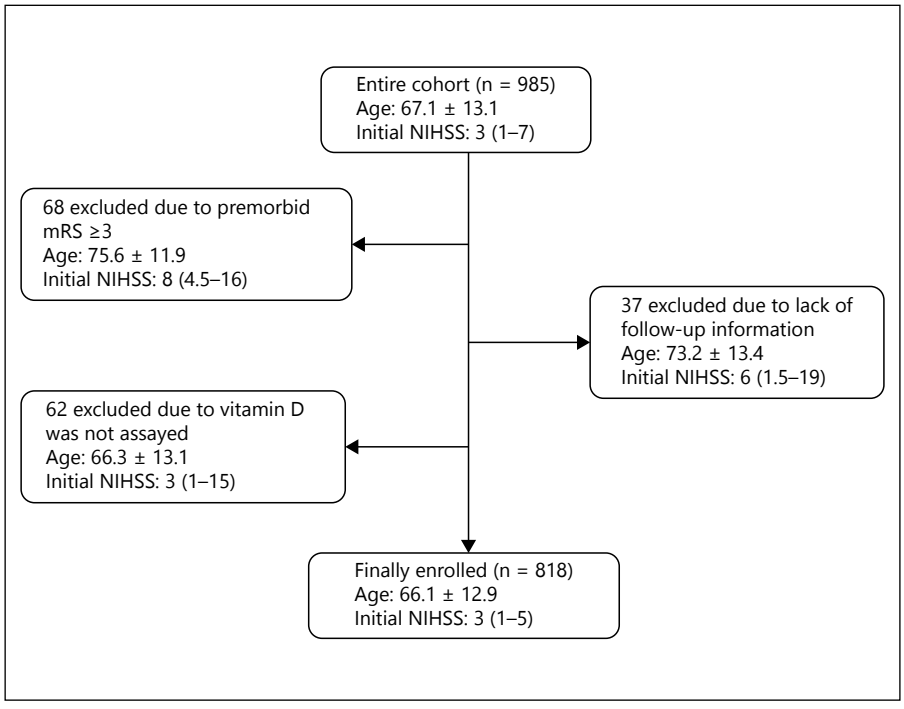

Fig. 1. Flow diagram of study participants with age (mean ± SD) and initial NIHSS score (median, IQR).

tion in 25(OH)D concentrations, we assigned individuals to percentiles of 25(OH)D concentration according to their month of admission. 25(OH)D was also categorized using the absolute level of 25(OH)D. According to the Endocrine Society guidelines, we defined the optimal vitamin D level as a level of 25(OH)D >75 nmol/l. Vitamin D insufficiency set at a 25(OH)D level between 50 and 75 nmol/l, while vitamin D deficiency was defined as a 25(OH)D level <50 nmol/l [16]. Severely deficient status was set at a 25(OH)D level <25 nmol/l.

Cerebrovascular Risk Factors

The following risk factors were considered: (1) hypertension, which was defined as the use of antihypertensive medication or blood pressure reading of ≥140/90 mm Hg on repeated measurements at least 1 week after stroke onset; (2) diabetes mellitus, defined as the use of diabetic medication, a fasting glucose level ≥7 mmol/l or a 2-hour serum glucose ≥11.1 mmol/l; (3) current cigarette smoking; (4) hypercholesterolemia, defined as the use of a cholesterol-lowering agent or a fasting cholesterol level ≥5.7 mmol/l; (5) a history of coronary artery disease; (6) a history of stroke and (7) a history of atrial fibrillation or newly detected atrial fibrillation during admission.

Statistical Analysis

Baseline characteristics were compared between those with good and poor outcomes using the χ^2 test, the Student t test, the analysis of variance (ANOVA) or the Kruskal-Wallis test, as appropriate. We also compared the characteristics among month-specific 25(OH)D quartiles and absolute values of 25(OH)D separately. Multivariable analyses were performed via multiple logistic regression to determine the association between 25(OH)D and 3-month functional outcomes. In multivariable analysis, variables with p values <0.2 from the univariate analysis and biologically plausible variables were selected as potential confounders for statistical adjustment. In Model 1, analyses were adjusted for age, sex and 25(OH)D. In Model 2, analyses were additionally adjusted for hypertension, diabetes, atrial fibrillation, stroke history, leukocyte count, hemoglobin, fasting glucose and fasting triglyceride level. Analyses were further adjusted in Model 3 for admission National Institute of Health Stroke Scale (NIHSS) score and stroke subtypes. All analyses were performed using PASW statistics 17.0 (SPSS Inc., Chicago, Ill., USA).

Results

Basic Characteristics

In all, 818 patients were included in the analysis. Their mean age was 66.2 (±12.9) years, and 40.5% were female (table 1). The mean 25(OH)D level was 47.2 ± 31.7 nmol/l, and the majority of patients met vitamin D deficient status (<50 nmol/l; 68.8%), while an optimal vitamin D level (≥75 nmol/l) was present in only 13.6% of the patients. There were seasonal variations in 25(OH)D levels, with the highest values found in the summer season in June (n = 75, 60.2 ± 42.2 nmol/l) and the lowest values being observed in March (n = 50, 38.9 ± 22.0 nmol/l, p = 0.013) and in January (n = 82, 39.9 ± 26.7 nmol/l, p = 0.004). To adjust for the seasonal variation of 25(OH)D levels, 25(OH)D quartiles were calculated for each calendar month, and the mean 25(OH)D levels for each quartile were 20.2, 34.0, 46.7 and 88.1 nmol/l from the lowest to the highest quartiles. Participants with higher 25(OH)D quartiles were more likely male subjects and had lower mean mRS scores at 3 months, higher mean hemoglobin, higher total cholesterol and higher triglyceride levels (table 2). These clinical characteristics were similar when the 25(OH)D level was categorized by the absolute level (table 3).

Stroke Outcome

Good functional outcome (mRS ≤2) at 3 months was achieved in 436 patients (53.3%). Serum 25(OH)D levels in patients with good outcomes were significantly higher than in those with unfavorable outcomes (50.2 ± 32.7 vs. 43.9 ± 30.0 nmol/l, p = 0.007). Other characteristics associated with unfavorable outcomes in univariate analysis were higher age, female sex, the presence of diabetes, atrial fibrillation, higher admission NIHSS score, lower hemoglobin, higher fasting glucose, higher high-sensitivity C-reactive protein and low triglyceride level (table 1).

The 3-month functional outcome was significantly associated with month-specific 25(OH)D quartiles in multivariable logistic regression analysis (table 4). After adjustment for age and sex, patients in the highest 25(OH)D quartile had higher tendency for good functional outcome at 3 months: the odds ratio (OR) (95% confidence interval (CI) for good functional outcome was 1.68 (1.13–2.51). After fully adjusting for other potential confounders, the association was further strengthened with an OR (95% CI) of 1.90 (1.14–3.16). This relationship is dose-responsive since increasing OR values were observed along with increments of quartile ranges. This association was also demonstrated when the 25(OH)D levels were categorized according to absolute values. Patients with optimal 25(OH)D level (≥75 nmol/l) showed higher tendency for good functional outcome compared with those who had severely deficient 25(OH)D levels (OR = 2.29, 95% CI = 1.22–4.31). Other factors associated with good functional outcome in multivariable analysis were younger age, lower initial NIHSS score and absence of diabetes.

Discussion

The present study demonstrated that low 25(OH)D levels were associated with poor functional outcomes in patients with acute ischemic stroke as analyzed by both

Table 1. Comparison of general characteristics according to 3-month functional outcome

Characteristics	Overall (n = 818)	Good outcome (n = 436)	Poor outcome (n = 382)	p value
25(OH)D, nmol/l	47.2±31.7	50.2±32.7	43.9±30.0	0.007
Age, years	66.2±12.9	64.2±12.4	68.4±13.2	<0.001
Female sex	40.5	36	46	0.006
Hypertension	71.0	70.9	71.2	0.917
Diabetes mellitus	38.3	32.6	44.8	<0.001
Hyperlipidemia	30.9	30.7	31.2	0.897
Coronary heart disease	11.9	12.9	10.8	0.352
Atrial fibrillation	21.9	17.5	27.0	0.001
History of stroke	15.2	13.3	17.3	0.114
Current smoking	29.3	30.9	27.5	0.294
Admission NIHSS, median (IQR)	3 (1–5)	2 (1–3)	4 (3–10)	<0.001
Leukocyte, 10^9/l	8.1±2.8	7.9±2.6	8.3±2.9	0.084
Hemoglobin, g/l	138±19	140±19	136±21	0.001
Fasting glucose, mmol/l	7.7±3.2	7.4±3.0	8.0±3.5	0.016
HbA1c	6.4±1.3	6.3±1.2	6.5±1.4	0.008
Total cholesterol, mmol/l	4.4±1.1	4.4±1.0	4.3±1.1	0.804
Low-density lipoprotein, mmol/l	2.6±1.0	2.6±1.0	2.7±1.0	0.89
Triglyceride, mmol/l	3.4±2.1	3.5±2.2	3.2±2.1	0.028
High-density lipoprotein, mmol/l	1.2±0.3	1.1±0.3	1.2±0.3	0.368
High-sensitivity C-reactive protein, mg/dl	0.30±0.46	0.22±0.34	0.40±0.56	<0.001
Stroke subtypes				0.002
Small vessel occlusion	22.1	25.5	18.2	
Large artery disease	25.8	23.7	28.2	
Cardioembolism	22.3	18.3	26.8	
Undetermined etiology and other etiology	29.8	32.5	26.8	

Values are % or mean ± SD unless otherwise indicated. Values are calculated by χ^2 test, Student t test, or Mann-Whitney U test as appropriate.

month-specific quartiles and the absolute level of 25(OH)D. Vitamin D deficiency (defined by 25(OH)D level <50 nmol/l) was highly prevalent in the current study, exceeding 68% while only 13.6% of participants had optimal vitamin D level. These findings were consistent with those of previous studies, which showed 68–78% prevalence of vitamin D deficiency in the Chinese acute ischemic stroke population [14, 15]. Our findings have confirmed the results of the previous studies, which suggested that 25(OH)D is a prognostic marker of functional outcome and death in patients with acute ischemic stroke and hemorrhagic stroke [13, 14].

Several studies have focused on the relationship between stroke and vitamin D. In a cross-sectional study, vitamin D levels were significantly lower in patients with acute stroke compared with those in controls [17, 18]. Low level of vitamin D has been associated with an increased future risk of stroke and acute myocardial infarction during 10 years of follow-up [19] and was independently predictive for fatal stroke in patients who were referred for coronary angiography at baseline [20]. In a prospective population-based cohort study, individuals with severe 25(OH)D deficiency (<25 nmol/l) had higher risk of ischemic stroke (hazard ratio 1.36, 95% CI 1.09–1.70) compared with individuals with optimal 25(OH)D level (>75 nmol/l) during 21 years of follow-up [21]. Interestingly, hemorrhagic stroke was not associated with vitamin D status in that study.

Recently, a few studies have tried to demonstrate the association between vitamin D status and functional outcome of acute stroke. Low 25(OH)D level was a predictor of functional outcome at discharge [13] and 1-year mortality [22] in Caucasian stroke population. However, both results were derived from an identical cohort. Serum 25(OH)D level was a predictor of both the severity at admission and the discharge functional outcome in Chinese patients with acute ischemic stroke [15]. Another study suggested low 25(OH)D level as an

Table 2. Patients' characteristics according to month specific quartiles

Number of patients	Lowest quartile (n = 204)	2nd quartile (n = 205)	3rd quartile (n = 205)	Highest quartile (n = 205)	p value
25(OH)D, nmol/l	20.2±7.0	34.0±6.2	46.7±7.0	88.1±35.9	<0.001
Age, years	66.4±14.8	65.9±12.4	66.2±12.4	66.3±12.1	0.988
Female sex	49.0	36.1	40.0	36.6	0.029
Hypertension	68.1	71.2	74.6	69.8	0.529
Diabetes mellitus	41.2	34.2	43.4	34.2	0.114
Hyperlipidemia	32.4	27.3	30.2	33.7	0.514
Atrial fibrillation	17.7	28.8	22.4	18.5	0.026
Coronary artery disease	12.8	11.7	13.2	9.8	0.736
History of stroke	18.1	14.2	13.7	14.6	0.58
Current smoking	26.2	33.2	30.4	27.7	0.442
Admission NIHSS	3 (1–5)	2.5 (1–5)	3 (1–5)	3 (1–6)	0.891
mRS at 90 day					
Mean ± SD	2.8±1.5	2.4±1.5	2.5±1.4	2.3±1.4	0.001
Median (IQR)	3 (2–4)	2 (1–3)	2 (1–3)	2 (1–3)	0.002
Leukocyte, 10^9/l	8.2±3.0	8.1±2.7	8.4±3.0	7.7±2.2	0.066
Hemoglobin, g/l	133±22	138±19	141±16	141±16	<0.001
Fasting glucose, mmol/l	8.1±3.7	7.7±3.2	7.8±3.3	7.3±2.7	0.116
HbA1c	6.6±1.5	6.2±1.0	6.5±1.4	6.3±1.1	0.051
Total cholesterol, mmol/l	4.2±1.2	4.2±1.0	4.5±1.0	4.5±1.0	0.003
Low density lipoprotein, mmol/l	2.6±1.0	2.6±1.0	2.7±0.9	2.8±1.0	0.221
High density lipoprotein, mmol/l	1.1±0.3	1.1±0.3	1.2±0.3	1.2±0.3	<0.001
Triglyceride, mmol/l	3.0±1.5	3.4±2.3	3.4±2.2	3.8±2.4	0.001
High-sensitivity C-reactive protein, mg/dl	0.34±0.49	0.32±0.46	0.31±0.50	0.24±0.40	0.181
Stroke subtypes					0.403
Small vessel occlusion	23.3	19.7	22.9	22.4	
Large artery disease	24.2	24.6	26.8	27.4	
Cardioembolism	21.3	29.6	20	18.4	
Undetermined etiology and other etiology	31.2	26.1	30.3	31.8	

Values are %, mean ± SD, or median (IQR). Values are calculated by χ^2 test, ANOVA, or Kruskal-Wallis test as appropriate.

independent predictor of poor functional outcome at 90 days in acute ischemic stroke [14]. The present study substantiated the association of 25(OH)D level and stroke outcome since our study had a larger sample size and excluded previously disabled patients (defined by mRS ≥3). Premorbid functional status might strongly affect both the stroke outcome (premorbid patients generally have poorer outcomes after incident stroke) and 25(OH)D level (premorbid patients potentially have low 25(OH)D level due to decreased sunlight exposure).

Several plausible pathophysiologic mechanisms underlying the association between low 25(OH)D level and stroke outcome could be speculated. Both animal and clinical studies have suggested that the infarct volume is larger in participants with low vitamin D levels. Rat model fed with vitamin D-deficient diet had significantly larger infarct size and more severe behavioral changes compared with the controls [23]. There was a negative correlation between the level of 25(OH)D and the infarct volume in patients with acute ischemic stroke [15]. It has been well established that the infarct volume is closely related with initial neurological deficits and is a strong prognostic marker for predicting stroke outcome. It has also been suggested that the initial neurological deficit is more severe in patients with lower 25(OH)D status [13, 15]. The present study demonstrated a strong association between the initial neurological severity defined by NIHSS score and the functional outcome. However, there were no differences of initial NIHSS score among each quartile of 25(OH)D in our cohort. Therefore, the initial infarct severity may not explain all the associations between 25(OH)D and stroke outcome. Vitamin D deficiency is known be associated with poorer cognitive function and dementia [24]. As a result, vitamin D deficiency-induced cognitive decline might play a role in

Table 3. Patients characteristics according to absolute vitamin D level status

	Severe deficiency (<25 nmol/l)	Deficiency (25–49.9 nmol/l)	Insufficiency (50–74.9 nmol/l)	Optimal (≥75 nmol/l)	p value
Number of patients	161 (19.7)	402 (49.1)	144 (17.6)	111 (13.6)	
25(OH)D, nmol/l	17.5±5.5	37.2±7.2	60.7±7.5	109.1±37.2	<0.001
Age, years	66.8±14.1	65.8±13.1	66.6±11.3	66.2±12.8	0.832
Female sex	50.3	38.6	36.8	37.8	0.042
Hypertension	65.8	73.4	71.5	69.4	0.34
Diabetes mellitus	40.4	37.8	45.8	27.0	0.021
Hyperlipidemia	32.3	29.9	27.8	36.9	0.407
Atrial fibrillation	22.4	23.9	16.7	20.9	0.339
Coronary artery disease	11.8	12.2	10.4	12.6	0.937
History of stroke	19.9	13.2	11.8	19.8	0.068
Current smoking	27.5	29.8	31.8	27.5	0.835
Admission NIHSS	3 (1–5)	3 (1–5)	3 (1–6)	3 (1–7)	0.239
mRS at 90 day					
Mean ± SD	2.9±1.5	2.4±1.5	2.4±1.4	2.4±1.4	0.004
Median (IQR)	3 (2–4)	2 (1–3)	2 (1–3)	2 (1–3)	0.008
Leukocyte, 10^9/l	8.0±2.9	8.3±2.8	8.0±2.9	7.8±2.2	0.364
Hemoglobin, g/l	132±23	139±18	140±16	141±17	<0.001
Fasting glucose, mmol/l	7.8±3.4	7.8±3.4	7.8±3.2	6.9±2.1	0.062
HbA1c	6.5±1.5	6.4±1.3	6.5±1.3	6.3±1.1	0.381
Total cholesterol, mmol/l	4.1±1.1	4.4±1.1	4.5±1.0	4.6±1.0	0.001
Low density lipoprotein, mmol/l	2.5±1.0	2.7±0.9	2.7±0.9	2.8±1.0	0.032
High density lipoprotein, mmol/l	1.1±0.3	1.1±0.3	1.2±0.4	1.2±0.4	0.012
Triglyceride, mmol/l	2.8±1.4	3.4±2.2	3.6±2.1	4.0±2.5	<0.001
hs-CRP, mg/dl	0.33±0.51	0.31±0.45	0.27±0.49	0.27±0.42	0.582
Stroke subtypes					
Small vessel occlusion	20.9	21.7	26.6	19.3	
Large artery disease	23.4	25.7	26.6	28.4	
Cardioembolism	26.0	23.9	15.4	20.2	
Undetermined etiology and other etiology	29.8	28.7	31.5	32.1	

Values are %, mean ± SD, or median (IQR). Values are calculated by χ^2 test, ANOVA, or Kruskal-Wallis test as appropriate.

Table 4. OR (95% CI) of 3-month good outcome (mRS = 0, 1, 2) for 25(OH)D according to month-specific quartiles of 25(OH)D and absolute 25(OH)D level status

Serum 25(OH)D	Model 1		Model 2		Model 3	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Lowest quartile	1 (Reference)		1 (Reference)		1 (Reference)	
2nd quartile	1.43 (0.96–2.12)	0.079	1.52 (0.96–2.40)	0.075	1.40 (0.85–2.31)	0.188
3rd quartile	1.48 (0.99–2.20	0.054	1.62 (1.03–2.55)	0.038	1.66 (1.01–2.73)	0.047
Highest quartile	1.68 (1.13–2.51)	0.011	1.70 (1.07–2.69)	0.025	1.90 (1.14–3.16)	0.014
<25 nmol/l	1 (Reference)		1 (Reference)		1 (Reference)	
25–50 nmol/l	1.52 (1.04–2.21)	0.03	1.47 (0.96–2.26)	0.079	1.32 (0.82–2.11)	0.250
50–75 nmol/l	1.5 (0.95–2.38)	0.083	1.56 (0.92–2.63)	0.097	1.80 (1.00–3.23)	0.050
≥75 nmol/l	2.02 (1.22–3.33)	0.006	1.98 (1.11–3.51)	0.020	2.40 (1.25–4.62)	0.009

Model 1 includes age, sex and 25(OH)D. Model 2 includes model 1 and adds hypertension, diabetes, atrial fibrillation, stroke history, leukocyte count, hemoglobin, fasting glucose, high-sensitivity C-reactive protein and fasting triglyceride level. Model 3 includes model 2 and admission NIHSS score and stroke subtypes.

causing unfavorable functional outcome in stroke patients.

Inflammation has a significant role in the pathogenesis of ischemic stroke. Vitamin D may exert anti-inflammatory effects, and post-stroke inflammatory response might be augmented in patients with vitamin D deficiency [23]. Laboratory studies have demonstrated that vitamin D suppresses inflammation through several pathways, including inhibiting prostaglandin and cyclooxygenase 2 pathways, reducing matrix metalloproteinage-9 and upregulating anti-inflammatory cytokine [25, 26].

Leukoaraiosis is associated with poor functional outcome after ischemic and hemorrhagic stroke [27, 28]. A recent study showed that the severity of chronic small vessel disease, including leukoaraiosis, is inversely associated with the 25(OH)D level in patients with ischemic stroke [29]. Therefore, underlying small vessel disease might affect the outcome status in patients with low vitamin D level.

Vitamin D deficiency-induced derangement of bone metabolism is another potential mechanism of poor outcome in post-stroke patients. Studies have indicated that vitamin D deficiency is associated with reduced bone mineral density in stroke patients, which might influence their functional outcome [30]. A small randomized trial suggested that vitamin D supplementation may prevent falls and fractures in chronic stroke patients [31].

The limitations of this study should be mentioned. First, this was a retrospective cross-sectional study. Therefore, causality between the 25(OH)D level and the stroke outcome could not be definitively addressed in our cross-sectional analysis and remains to be determined by future randomized controlled trials. Second, serum 25(OH)D level can be increased by outdoor physical activity, and premorbid physical activity might be positively associated with the functional outcome of stroke [32]. In contrary, frailty could reduce 25(OH)D level and negatively influence the outcome. Therefore, 25(OH)D level might only represent premorbid functional status and be a mere innocent bystander between the premorbid physical health and the post-stroke outcome. Although we excluded patients with pre-stroke mRS ≥3, pre-stroke outdoor activity and frailty scale were not considered in the present analysis. Third, this study was conducted in patients from a purely Korean ethnic background. Several studies have suggested racial differences of association between vitamin D and CVD. Therefore, the results of this study might not be generalizable to other ethnic populations. Last, other unmeasured factors might have accounted for the relation between vitamin D and stroke prognosis such as obesity and parathyroid hormone [33, 34]. However, body mass index and parathyroid hormone level were not routinely checked and not analyzed in the present study.

In conclusion, our study suggests that the serum 25(OH)D level status is associated with the functional outcome in patients with acute ischemic stroke. Although vitamin D research has increased substantially, the benefits of this hormone remain to be determined. Further studies are required to determine whether vitamin D supplementations might be of benefit to patients with acute ischemic stroke.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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