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Effects of native vitamin D supplementation on vitamin D status and body composition after sleeve gastrectomy: A retrospective study in Japanese patients

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A R T I C L E I N F O

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A B S T R A C T

Introduction: The effect of vitamin D status after bariatric surgery on postoperative skeletal muscle condition has not been adequately studied.
Methods: Clinical data from 83 patients (median age 44 years, BMI 40.4 kg/m^2) who underwent sleeve gastrectomy (SG) were collected from medical records and analyzed retrospectively. Of the 83 patients, 37 who received continuous guidance on native vitamin D3 supplementation from before to 12 months after surgery were defined as the vitamin D supplementation (VDS) group, and 46 patients who did not receive such guidance as the control group. Native vitamin D3 supplement was provided by a dietitian at preoperative and postoperative visits. The supplementation dose was prescribed at 3000 IU/day after SG.
Results: In VDS group, blood 25-hydroxyvitamin D (25OHD) level increased significantly from 18.5 at baseline to 29.7 ng/mL at 3 months after surgery and plateaued, while 25OHD level remained low in the control group. In the analysis that included both groups, change in 25OHD level from baseline to 12 months after surgery correlated significantly with mean vitamin D intake ($r = 0.596$, $p < 0.001$) and 12-month post-SG/baseline ratio of percent lower limb skeletal muscle mass ($r = 0.469$, $p < 0.05$). Multiple regression analysis identified change in 25OHD level and mean exercise time as significant factors independently associated with 12-month post-SG/baseline ratio of percent lower limb skeletal muscle mass.
Conclusion: Vitamin D3 supplementation after SG is useful for improving vitamin D status that may be associated with prevention of postoperative lower limb skeletal muscle mass loss.

1. Introduction

Vitamin D deficiency is not only associated with the well-known adverse effect on bone metabolism, but also contributes to sarcopenia [1]. Blood 25-hydroxyvitamin D (25OHD) level is widely used as an indicator reflecting the status of vitamin D metabolism in the body [2], and a 25OHD level below 20 ng/mL is generally defined as vitamin D deficiency, while a level between 20 ng/mL and 30 ng/mL as vitamin D insufficiency [3]. Individuals with obesity are known to have low 25OHD levels and a high frequency of vitamin D deficiency or insufficiency, and the more severe the obesity, the higher is the frequency [4]. Therefore, the frequency of vitamin D deficiency and insufficiency is extremely high in patients with severe obesity having BMI >35 kg/m^2 [5].

Bariatric surgery is widely recognized as an effective treatment to achieve significant and sustained weight loss in patients with severe obesity [6,7]. While vitamin D status has been reported to improve when patients with obesity lose weight through lifestyle modification [8], the

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situation is different when weight loss results from bariatric surgery. Despite significant weight loss after bariatric surgery, vitamin D status does not improve but worsens instead [9,10]. Sleeve gastrectomy (SG) is currently the most common procedure [11] and, unlike gastric bypass, has minimal impact on the digestive and absorptive functions of the gastrointestinal tract [12]. However, the rate of postoperative vitamin D deficiency/insufficiency is still high after SG, and the frequency has been reported to be similar to that of gastric bypass [13]. The updated guidelines for perioperative support of bariatric surgery patients co-sponsored by American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic and Bariatric Surgery (AACE/TOS/ASMBS) recommend vitamin D supplementation after surgery based on accumulated evidence and explicitly state an intake of 3000 IU/day [14]. On the other hand, vitamin D status is known to vary widely by geographical region, as it is affected by race, skin color, and other factors [15]. Compared to the evidence accumulated in European and Northern American countries, there is a lack of studies of vitamin D status after bariatric surgery in Asian countries including Japan, and the actual situation is not sufficiently clear.

Furthermore, skeletal muscle mass is reduced after bariatric surgery, accompanying the significant loss of body fat [16,17]. Since postoperative loss of skeletal muscle mass is associated with weight regain and is a risk factor for sarcopenic obesity, it is important to minimize the extent of muscle loss. Studies have elucidated that vitamin D status is closely related to skeletal muscle mass and function [18,19]. Therefore, the deterioration of vitamin D status after bariatric surgery may have an adverse effect of postoperative skeletal muscle loss. However, the relationship between the change in vitamin D status and body composition, including skeletal muscle, after bariatric surgery has not been adequately investigated. To clarify the potential role of vitamin D after bariatric surgery, we investigated the relationship between the vitamin D status and body composition, as well as the vitamin D intake in Japanese patients who underwent SG.

2. Methods

2.1. Study protocol

In April 2014, screening for blood 25OHD level, an indicator reflecting the status of vitamin D metabolism, in patients with severe obesity was started at Toho University Sakura Medical Center (Sakura City, Chiba, Japan). Since April 2016, physicians have instructed patients with vitamin D deficiency or insufficiency to take native vitamin D3 supplement. In the present study, we retrospectively reviewed the clinical records at the Center from April 2014 to March 2019 to identify patients who underwent SG and were followed for at least 12 months after surgery. In Japan, the criterion for a valid indication for SG is BMI $\geq$32 kg/m^2 with at least one obesity-related comorbidity, such as type 2 diabetes, hypertension, or dyslipidemia; or BMI $\geq$35 kg/m^2, according to the guideline of the Japanese Society for the Treatment of Obesity [20]. We excluded patients whose body composition was not measured, and those with insufficient blood samples for the analyses at baseline and/or at 12 months after SG.

Of 103 patients who met the above criteria, we excluded 17 patients who started native vitamin D3 supplementation after undergoing SG. We further excluded 3 patients (3 of 86, 3.5 %) with preoperative 25OHD levels in the range of vitamin D sufficiency (>30 ng/mL). Finally, the clinical data of 83 patients were collected from medical records and analyzed retrospectively. Thirty-seven of the 83 patients who received continuous native vitamin D3 supplementation guidance from before SG to 12 months after SG were defined as the vitamin D supplementation group, and 46 patients who did not receive such guidance were defined as the control group. The flowchart for patient enrollment is shown in Fig. 1.

The native vitamin D3 supplement was a commercial product (DHC corporation, Tokyo, Japan). A dietitian introduced the product to the subjects, and encouraged them to purchase and take by themselves. The supplementation dose after SG was prescribed at 3000 IU/day. The

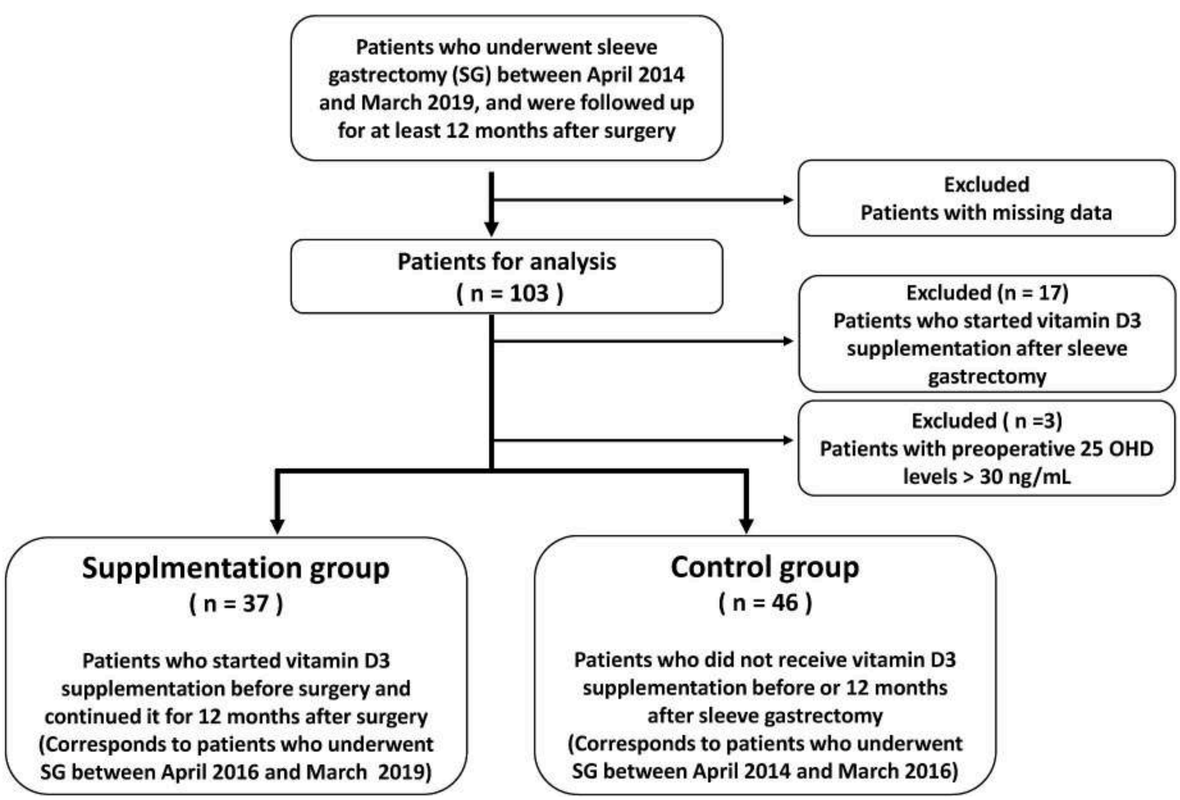

Fig. 1. Flowchart of patient registration in this research.

actual doses taken were obtained from the records of dietary interviews conducted by the dietitian during visits. Other information on dietary vitamin D intake and amount of physical activity was also collected. The supplementation dose was reduced to 2000 IU/day if 25OHD level was higher than 50 ng/mL at 3 or 6 months after SG, and increased to 4000 IU/day if the 25OHD level was lower than 10 ng/mL.

Weight measurements and collection of blood and urine samples were performed in the morning after a 12-h fast. In this study, we evaluated the following parameters: body weight (BW); body mass index (BMI); visceral fat area (VFA); subcutaneous fat area (SFA); and blood levels of aspartate transaminase (AST), alanine transaminase (ALT), γ-glutamyl transpeptidase (GTP), serum creatinine, fasting plasma glucose (FPG), hemoglobin A1c (HbA1c), parathyroid hormone (PTH) intact and 25OHD.

The protocol of the study was prepared and implemented in accordance with the tenets of the Declaration of Helsinki, and was reviewed and approved by the Ethics Committee of Toho University Sakura Medical Center (approval date: August 6, 2021, approval number: S21023). Although this was a retrospective study, we explained to individual patients for usage and release of study data and obtained written consent from each patient.

2.2. Measurement of blood samples

To measure HbA1c, blood was collected in tubes containing ethylenediaminetetraacetic acid. The stable and unstable fractions of HbA1c were measured by high-performance liquid chromatography using a Hi-Auto A1c Analyzer (Kyoto Daiichi Kagaku, Kyoto, Japan). Data for the stable form were used in the present analysis. HbA1c was expressed as that of the National Glycohemoglobin Standardization Program. The levels of 25-OHD and PTH intact were analyzed at LSI Medience Corporation (Tokyo, Japan), and were measured by electrochemiluminescence immunoassay.

2.3. Measurement of anthropometric factors

To determine the VFA, a computed tomography scan (Aquilion ONE, Canon Medical Systems Co., Japan) was performed at the umbilical level with the patient supine. The SFA was calculated by subtracting VFA from the total fat area. Radiologists quantified the fat area using Ziostation 2 software version 2.9.7.1 (Ziosoft, Inc., Tokyo, Japan). Body composition was analyzed using a bioelectrical impedance analysis system (InBody 720, InBody Japan) that measures the body weight, skeletal muscle mass, appendicular muscle mass, trunk muscle mass, and fat mass. Using the system, the impedance in the right arm, left arm, trunk, right leg, and left leg was measured separately at six different frequencies (1, 5, 50, 250, 500, and 1000 kHz, respectively). Body composition variables were calculated by dividing the parameters by the body weight to obtain percent fat mass, percent skeletal muscle mass, percent upper limb muscle mass, percent trunk muscle mass, and percent lower limb muscle mass.

2.4. Statistical analysis

Data are expressed as median (interquartile range [IQR]). Statistical analysis was performed using Student's *t*-test and analysis of variance for data showing normal distribution determined by Shapiro-Wilk test. If the data did not show normal distribution, we analyzed the data using Wilcoxon test. Simple linear regression analysis and multiple regression analysis were performed using SPSS software version 26 (Armonk, NY, USA: IBM Corp.). In all analyses, p values less than 0.05 were considered significant.

3. Results

3.1. Baseline characteristics

Table 1 shows preoperative (baseline) clinical parameters of the two groups. The vitamin D supplementation and control groups had, respectively, male to female ratios of 16:21 and 23:23, median age of 48 and 44 years, median BMI of 40.4 and 41.3 kg/m^2, median 25OHD levels of 18.5 and 14.3 ng/mL, and median PTH intact of 47 and 48 pg/mL. There were no significant differences between the two groups in all the parameters.

3.2. Changes in 25OHD and PTH intact levels during 12 postoperative months

Median daily vitamin D intake (sum of supplementation and dietary intake) over the 12-month postoperative period was 2520 IU in the supplementation group and 328 IU in the control group. There were no significant differences between the two groups in daily energy intake, protein intake, and physical activity time during the 12-month period (Table 2).

In the supplementation group, median 25OHD level increased significantly from 18.5 ng/mL before SG to 29.7 ng/mL at 3 months after SG but did not reach the sufficiency level of 30 ng/mL, and then plateaued at 28.8 ng/mL at 6 months and 28.2 ng/mL at 12 months after SG. The 25OHD level in the control group remained low with no significant changes until 12 months after SG (Fig. 2).

The change in 25OHD level during the 12-month postoperative period was significantly greater ($p < 0.001$) in the supplementation group (+8.0 ng/mL) than in the control group (−0.3 ng/mL) (Table 2). The proportions of patients with 25OHD levels above the vitamin D deficiency (below 20 ng/mL) and insufficiency (20–30 ng/mL) ranges at 12 months after SG were 72.4% and 41.3%, respectively, in the supplementation group, and 19.5 %, 4.8 % in the control group. The PTH intact level showed a decreasing trend (−3.0 pg/mL) in the supplementation group, while there was no significant change in the control group (+2.0 pg/mL), and the change in PTH intact was not significantly different between the two groups (Table 2).

3.3. Adverse events

During the study period in the supplementation group, there were no cases where 25OHD levels exceeded 80 ng/mL, and there were no new cases of hypercalcemia, hypercalciuria, or urinary tract stones. There were no cases of fracture in either group. However, since bone metabolism parameters were not collected in this study, the data related to this were unclear.

3.4. Changes in body composition parameters during 12 postoperative months

Percent body weight, BMI, VFA, SFA, and body fat decreased significantly at 12 months after SG compared to before SG in both the vitamin D supplementation and control groups, but the amounts of reduction in these parameters did not differ significantly between the two groups (Table 2). The 12-month post-SG to baseline ratio of percent skeletal muscle mass for the whole body as well as for upper and lower limbs increased in both groups, but there were no significant differences in the amounts of change between the two groups (Table 2).

3.5. Changes in blood pressure, parameters of glucose metabolism, liver and kidney functions during 12 postoperative months

Systolic blood pressure, diastolic blood pressure, FPG, HbA1c, AST, ALT and GTP decreased significantly, and serum creatinine did not change in both groups. Changes in all the parameters were not

Table 1
Comparison of preoperative clinical parameters in vitamin D supplementation (VD supple) group and no vitamin D supplementation (control) group.

		VD supple group		Control group		*p value*
		median	(IQR)	median	(IQR)	
age	(yrs)	**48**	(41–50)	**44**	(39–52)	n.s.
Sex ratio	(m/f)	**16/21**		**23/23**		n.s.
body weight	(kg)	**110**	(94–137)	**109**	(96–119)	n.s.
body mass index	(kg/m^2)	**40.4**	(37.8–37.7)	**41.3**	(37.0–45.7)	n.s.
visceral fat area	(cm^2)	**222**	(140–296)	**211**	(177–260)	n.s.
subcutaneous fat area	(cm^2)	**431**	(401–542)	**467**	(401–588)	n.s.
percent skeletal muscle mass						
(whole body)	(%)	**27.2**	(25.9–31.9)	**28.2**	(26.8–31.2)	n.s.
(upper limb)	(%)	**3.1**	(2.9–3.2)	**3.3**	(2.8–3.4)	n.s.
(lower limb)	(%)	**10.1**	(8.6–11.7)	**9.5**	(9.1–9.9)	n.s.
percent fat (whole body)	(%)	**49.3**	(42.8–50.8)	**49.1**	(40.7–41.9)	n.s.
systolic blood pressure	(mmHg)	**133**	(124–144)	**136**	(127–147)	n.s.
diastolic blood pressure	(mmHg)	**80**	(75–92)	**83**	(78–90)	n.s.
fasting plasma glucose	(mg/dL)	**104**	(93–120)	**105**	(94–119)	n.s.
hemoglobin A1c	(%)	**6.1**	(5.8–6.7)	**6.4**	(5.8–7.3)	n.s.
aspartate transaminase	(IU/L)	**32**	(20–52)	**29**	(21–41)	n.s.
alanine transaminase	(IU/L)	**26**	(15–22)	**24**	(21–35)	n.s.
γ-glutamyl transpeptidase	(IU/L)	**31**	(26–52)	**34**	(22–43)	n.s.
creatinine	(mg/dL)	**0.7**	(0.6–0.8)	**0.7**	(0.6–0.8)	n.s.
25-hydroxyvitamin D	(ng/mL)	**18.5**	(11.8–23.3)	**14.3**	(11.9–17.9)	n.s.
parathyroid hormone intact	(pg/mL)	**47**	(36–56)	**48**	(36–72)	n.s.

Values are expressed as median (interquartile range [IQR]), n.s.; not significant.

Table 2
Comparison of vitamin D and nutrient intake, exercise, and changes in body composition parameters during 12 months after sleeve gastrectomy between vitamin D supplementation (VD supple) group and no vitamin D supplementation (control) group.

		VD supple. group		Control group		*p value*
		median	(IQR)	median	(IQR)	
vitamin D intake	(U/day)	**2520**	(1650–2779)	**328**	(192–390)	**<0.001**
energy intake	(kcal/day)	**1295**	(1009–1524)	**1250**	(1007–1618)	n.s.
protein intake	(g/day)	**62**	(42–65)	**61**	(54–74)	n.s.
exercise time	(hr/day)	**2.3**	(0–3.3)	**1.0**	(0–2.0)	n.s.
⊿ 25-hydroxyvitamin D	(ng/mL)	**8.0**	(1.1–20.0)	**−0.3**	(-2.6-3.8)	**<0.001**
⊿ parathyroid hormone intact	(pg/mL)	**−3.0**	(-14.0-6.0)	**2.0**	(-9.0- 10)	n.s.
⊿ body weight	(%)	**−28**	(-33 to −28)	**−26**	(-30 to −19)	n.s.
⊿ body mass index	(%)	**−28**	(-33 to −23)	**−26**	(-30 to −20)	n.s.
⊿ visceral fat area	(%)	**−54**	(-70 to −36)	**−51**	(-57 to −26)	n.s.
⊿ subcutaneous fat area	(%)	**−30**	(-47 to −18)	**−35**	(-49 to −23)	n.s.
percent skeletal muscle (whole body) (12M/baseline)		**1.2**	(1.1–1.3)	**1.3**	(1.2–1.4)	n.s.
percent skeletal muscle (upper limb) (12M/baseline)		**1.1**	(1.1–1.2)	**1.1**	(1.1–1.2)	n.s.
percent skeletal muscle (lower limb) (12M/baseline)		**1.3**	(1.2–1.3)	**1.3**	(1.2–1.4)	n.s.
percent fat (whole body) (12M/baseline)		**0.8**	(0.6–0.9)	**0.8**	(0.5–0.8)	n.s.
⊿ systolic blood pressure	(mmHg)	**−10**	(-21 to −6)	**−3**	(-19-4)	n.s.
⊿ diastolic blood pressure	(mmHg)	**−4**	(-14- 2)	**−2**	(-7-6)	n.s.
⊿ fasting plasma glucose	(mg/dL)	**−11**	(-27- 3)	**−8**	(-15-7)	n.s.
⊿ hemoglobin A1c	(%)	**−0.5**	(-1.0 to −0.3)	**−0.6**	(-1.1 to −0.3)	n.s.
⊿ aspartate transaminase	(IU/L)	**−17**	(-32 to −8)	**−13**	(-25 to −4)	n.s.
⊿ alanine transaminase	(IU/L)	**−8**	(-20 to −3)	**−6**	(-15 to −3)	n.s.
⊿ γ-glutamyl transpeptidase	(IU/L)	**−16**	(-30 to −8)	**−7**	(-20 to −2)	n.s.
⊿ creatinine	(mg/dL)	**0**	(-0.1- 0)	**−0.1**	(-0.1-0)	n.s.

Values are expressed as median (interquartile range [IQR]), n.s.; not significant, 12 M; 12 months after sleeve gastrectomy.

significantly different between the two groups.

3.6. Analysis of factors associated with change in blood 25OHD level

To explore the factors that determine the change in 25OHD level, we analyzed the correlation between the change of 25OHD level from baseline to 12 months after SG and various clinical parameters using univariate analysis in all patients (Table 3). Mean vitamin D intake over 12 months correlated strongly with the change in 25OHD level ($r = 0.596$, $p < 0.001$). Mean energy intake and protein intake, and changes in percent, BMI, VFA and SFA over the 12-month postoperative period did not correlate with the change in 25OHD level. On the other hand, 12-month post-SG/baseline ratio of percent lower limb skeletal muscle mass ("12-month/baseline ratio of lower limb skeletal muscle" hereinafter) correlated significantly with the change in 25OHD level ($r = 0.469$, $p < 0.05$).

3.7. Analysis of factors associated with 12-month/baseline percent lower limb skeletal muscle mass

To analyze factors independently associated with 12-month/baseline ratio of lower limb skeletal muscle, univariate and multivariate analyses were performed using 12-month/baseline ratio of lower limb skeletal muscle as the dependent variable (Table 4). In univariate analysis, 12-month/baseline ratio of lower limb skeletal muscle had a significant negative correlation with change in body weight ($r = -0.446$, $p < 0.05$), change in SFA ($r = -0.514$, $p < 0.05$), and change in 25OHD ($r = -0.469$, $p < 0.05$); and while it also showed a trend of association with

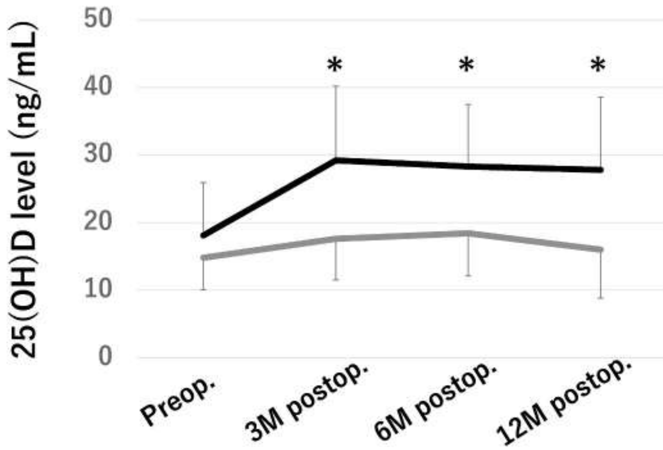

Fig. 2. Changes in 25-hydroxyvitamin D [25(OH)D] levels before and 3 months, 6 months and 12 months after sleeve gastrectomy. Black: vitamin D supplementation group, gray: control group. *p < 0.05 vs preop analyzed by repeated measures ANOVA.

Table 3
Univariate analysis of clinical variables associated with change in 25OHD level from baseline to 12 months after sleeve gastrectomy.

	r	*p* value
mean vitamin D intake/12M	**0.596**	**<0.001**
mean energy intake/12M	**0.076**	n.s.
mean protein intake/12M	**0.221**	n.s.
mean exercise time/12M	**−0.037**	n.s.
⊿ body mass index	**−0.270**	n.s.
⊿ visceral fat area	**−0.230**	n.s.
⊿ subcutaneous fat area	**−0.060**	n.s.
percent skeletal muscle (whole body) (12M/baseline)	**0.372**	n.s.
percent skeletal muscle (upper limb) (12M/baseline)	**0.333**	n.s.
percent skeletal muscle (lower limb) (12M/baseline)	**0.469**	**<0.05**
percent fat (whole body) (12M/baseline)	**−0.252**	n.s.

n.s.; not significant, 12 M; 12 months after sleeve gastrectomy.

Table 4
Univariate and multivariate analyses of clinical variables associated with 12-month post-SG/baseline ratio of percent lower limb skeletal muscle mass.

univariate	r	p value	
⊿ body weight	**−0.446**	**<0.05**	
⊿ body mass index	**−0.408**	0.074	
⊿ visceral fat area	**−0.389**	0.082	
⊿ subcutaneous fat area	**−0.514**	**<0.05**	
⊿ fasting plasma glucose	**−0.242**	n.s.	
⊿ HbA1c	**−0.290**	n.s.	
⊿ 25-hydroxyvitamin D	**0.469**	**<0.05**	
Mean exercise time	**0.165**	n.s.	
Mean energy intake	**−0.030**	n.s.	
Mean protein intake	**0.155**	n.s.	
Mean protein to energy ratio	**0.440**	0.092	
HbA1c; hemoglobin A1c, n.s.; not significant, SG; sleeve gastrectomy			
multivariate	β	t	p value
⊿ subcutaneous fat area	**0.322**	**1.203**	n.s.
⊿ 25-hydroxyvitamin D	**1.750**	**5.178**	**<0.05**
Mean exercise time	**1.625**	**4.374**	**<0.05**
Mean protein intake (% to energy)	**−0.960**	**−3.319**	n.s.
Adjusted $R^2 = 0.878$, SE = 0.066, $p < 0.05$			

change in BMI, change in VFA, and protein to energy ratio (12-month average), there was no statistical significance.

Multiple regression analysis with 12-month/baseline ratio of lower limb skeletal muscle as the dependent variable was conducted using mean exercise time previously reported to be related to skeletal muscle, in addition to variables having p values less than 0.1 in univariate analysis as independent variables. Change in 25OHD and mean exercise time were identified as factors independently associated with 12-month/baseline ratio of lower limb skeletal muscle.

4. Discussion

The primary result of this study is that despite similar significant decreases in body weight and body fat during the first 12 months after SG in both the vitamin D supplementation group and control (no supplementation) group, 25OHD levels in the control group remained low and unchanged, while 25OHD levels in the vitamin D supplementation group increased significantly by the third postoperative month and then plateaued until one year after SG. Patients with severe obesity are known to have a high prevalence of vitamin D deficiency or insufficiency [5]. Carasco et al. [21] reported that 31.6 %–92 % of patients who were candidates of bariatric surgery had vitamin D deficiency/insufficiency before operation. On the other hand, most of the previous reports were from European and Northern American countries, and very few reports have investigated the status of vitamin D in Asian patients who underwent bariatric surgeries, especially SG. This study is the first to clarify the status of vitamin D index in Japanese patients with severe obesity treated with SG. The frequencies of vitamin D deficiency and insufficiency in the patients in this study were extremely high; 96.5 % and 77.1 %, respectively, which are higher than previous reports from European and Northern American countries. Vitamin D status is known to differ among races with different skin colors [15], suggesting that vitamin D deficiency may be more severe in Asians than in Caucasians.

The present study also found that without vitamin D3 supplementation, vitamin D status did not improve after SG, even with significant weight and body fat loss. Vitamin D status is impaired in individuals with obesity due to multiple factors including changes in gastrointestinal hormones and immune cells, increased vitamin D catabolism in bone tissue, decreased sunlight exposure, and sequestration of vitamin D in adipose tissue, which result in lower 25OHD levels [22,23]. Study has shown that 25OHD increases after weight loss due to lifestyle modification [10]. However, it is also known that 25OHD levels do not increase during weight loss after bariatric surgery, because vitamin D metabolism is different from that in weight loss by other methods [9,10]. Traditionally, the main reason was presumed to be the changes in digestive and absorption kinetics due to surgical intervention in the gastrointestinal tract. Therefore, procedures with altered absorption kinetics, such as gastric bypass, were assumed to have greater impact on vitamin D metabolism than sleeve gastrectomy. However, more recent studies have reported that even SG has a similar effect on postoperative vitamin D metabolism as gastric bypass [13,24]. The results of the present study are consistent with previous findings, indicating that vitamin D supplementation and monitoring of vitamin D status are essential even after SG.

In the present study, an average intake of 2500 IU/day of vitamin D3 significantly increased 25OHD level after SG. Despite this increase, the average 25OHD level in the vitamin D supplementation group did not reach the vitamin D sufficiency level of 30 ng/mL, and only 41.3 % of the patients achieved the sufficiency level. Dix et al. [25] reported that vitamin D supplementation at 3000 IU/day prevented worsening of vitamin D metabolism in patients who underwent SG. AACE/TOS/ASMBS guidelines recommend 3000 IU/day vitamin D supplementation after bariatric surgery [14]. On the other hand, interventional studies of vitamin D supplementation after bariatric surgery using various protocols have been performed, but the frequency of achieving the vitamin D sufficiency range is not high [24,26]. In the present study, vitamin D3 supplementation at a dose of 3000 IU/day was prescribed to the subjects, but due to adherence issues and other factors, the final average dose taken by the patients was only 2500 IU/day. The results of this study suggest that the increase in 25OHD level is largely dictated by the dose of vitamin D3 supplementation. Given the increase in 25OHD level per unit of vitamin D3 supplementation in this study, we estimated that if intake of vitamin D 3000 IU/day could be achieved by solving various problems such as adherence, the average 25OHD level could exceed 30 ng/mL. In light of these considerations, 3000 IU/day of vitamin D3 supplementation may be appropriate for Japanese patients after undergoing SG for severe obesity. However, our findings also suggest that postoperative monitoring of vitamin D status is essential, as we estimate that some patients may not recover from vitamin D insufficiency.

Another major finding in this study was the association between change in 25OHD level and postoperative skeletal muscle loss in the lower limb. We found that change in 25OHD level from baseline to 12 months after SG was a factor independently associated with 12-month post-SG/baseline ratio of percent lower limb skeletal muscle mass. In addition, change in 25OHD level was strongly regulated by vitamin D supplementation. These findings suggest that maintaining high 25OHD levels with vitamin D supplementation may work toward preventing the loss of lower limb skeletal muscle mass after SG. After bariatric surgery, accompanying a significant loss of body fat, there is also a parallel loss of skeletal muscle mass [18]. Therefore, an important issue is how to prevent skeletal muscle mass loss after surgery. Maintaining protein intake and strengthening training are known to be effective in preventing postoperative skeletal muscle loss [27]. Recent studies have demonstrated a significant relationship between vitamin D metabolism and skeletal muscle mass and function. Visser et al. [28] reported an association between vitamin D deficiency/insufficiency and sarcopenia. Salles et al. [29] found that 25OHD levels are associated with skeletal muscle mass and function in animal models. Moreover, vitamin D supplementation has also been shown to contribute to improved skeletal muscle mass and function. A meta-analysis conducted by Tomlinson et al. [30] concludes that vitamin D supplementation improves upper and lower limb muscle strength in young healthy subjects. Another meta-analysis reported by Beaudart et al. [31] also shows a positive effect of vitamin D supplementation on muscle strength. The effects of vitamin D on skeletal muscle are considered to be mainly mediated through the vitamin D receptor. Girgis et al. [32] observed that skeletal muscle mass, muscle fiber size, and muscle strength were all reduced in myocyte-specific vitamin D receptor knockout mice, and Ceglia et al. [33] found that vitamin D supplementation increased muscle fiber size in older women, and that the mechanism involved upregulation of vitamin D receptors in skeletal muscle. In addition, vitamin D has been reported to affect myokines [34], and to be involved in skeletal muscle metabolism via mTORC1 signaling [35].

Despite the recent focus and research on the relationship between skeletal muscle and vitamin D metabolism, very few studies have examined this relationship in individuals with obesity or those after bariatric surgery, and the relationship has remained unclear. The results of this study demonstrate for the first time that improving vitamin D metabolism by vitamin D3 supplementation may prevent lower limb skeletal muscle loss after bariatric surgery. On the other hand, although the results of this study showed an association between 12-month post-SG/baseline ratio of percent lower limb skeletal muscle mass and vitamin D metabolism, no significant differences were detected between the vitamin D supplementation group and the control group. One possible reason may be the insufficient elevation of 25OHD levels in the vitamin D supplementation group. In any case, prevention of skeletal muscle loss after bariatric surgery is a very important matter, the results of this study suggest that vitamin D3 supplementation intervention may have a positive impact on there. In order to clarify these issues, it is necessary to conduct further investigation focusing on skeletal muscle with a more powerful protocol that would ensure an increase in 25OHD level to validate the present results.

5. Limitations

The first limitation of this study is that the two groups compared were treated at different times. The vitamin D supplementation group is the population that received SG after the start of supplementation instruction in April 2016, while the control group is the population that received SG at an earlier time. However, the LSG surgeon was the same throughout the treatment period for both groups, as well as the staff involved in the treatment, including the internists and dietitians who treated the patients. Second, this was a single-center, retrospective, observational study, and the results need to be validated by a multicenter, prospective study. Third, we were not able to collect data on the intake of calcium, exposure to ultraviolet rays, or the season in which the blood tests were conducted. Therefore, this study did not verify the possibility that these factors could have potentially affected 25 OHD levels. Finally, the results of this study do not allow determination of the optimal dose of vitamin D supplementation for Asian individuals undergoing SG. Determining the appropriate dose of vitamin D supplementation after SG for Asians is of great importance, and further investigations are warranted.

6. Conclusion

- Vitamin D deficiency/insufficiency is very common in Japanese patients undergoing sleeve gastrectomy.
- Vitamin D3 supplementation before and after sleeve gastrectomy is useful for improving the vitamin D status in Japanese patients with severe obesity.
- The effect of vitamin D3 supplementation before and after sleeve gastrectomy on 25 OHD levels is almost the same for Japanese as for Caucasians, and a dose of 3000 IU/d might be appropriate.
- Achievement or maintenance of good postoperative vitamin D status may be helpful with prevention of postoperative loss of lower limb skeletal muscle mass.
- Further studies focusing on skeletal muscle mass with a more powerful protocol that would ensure an increase in 25OHD level to validate the present results.

Author contribution (CRediT authorship contribution statement)

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Ethical review

The protocol of the study was prepared and implemented in accordance with the tenets of the Declaration of Helsinki. This study protocol was reviewed and approved by the Ethics Committee of Toho University Sakura Medical Center (approval date; August 6, 2021, approval number; S21023). Although this was a retrospective study, we explained to individual patients for usage and release of study data and obtained written consent from each patient.

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Declaration of AI and AI-assisted technologies in the writing process

No use of AI and AI-assisted technologies in this study.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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