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Vitamin D level as a predictor of dysmobility syndrome with type 2 diabetes

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Dysmobility Syndrome (DMS), is a combination, that is analogous to the approach taken with metabolic syndrome, The diagnosis of DMS is complex. So this study aimed to explore the relationship between 25-(OH) Vit D with Dysmobility Syndrome (DMS)in type 2 diabetes mellitus(T2DM) patients. This is a cross-sectional study, including 330 patients (67.0 ± 8.8 years old) with T2DM who were admitted to the Qinhuangdao First Hospital from October 2020 to February 2022. Selected independent variables include grip strength, six-meter gait speed, level of 25-(OH) vitamin D, and bone mineral density (BMD) measured by Dual-energy X-ray (DXA). DMS includes six conditions: osteoporosis, low muscle mass, low muscle strength, slow gait speed, occurrences of falls in the past year ≥ 1, and obesity, having three or more of these conditions were diagnosed with DMS. Patients were classified based on DMS. The detection rate of DMS in patients with T2DM was 25.5%. The proportion of vitamin deficiency is 67.9% in patients with T2DM. The 25-(OH) Vit D deficiency was defined based on the 25th percentile into two groups; < 36.2 nmol/L. The vitamin D levels in Group DMS were significantly lower than that in Group Non-DMS (41.74 ± 14.60 vs. 47.19 ± 13.01, *P* < 0.05). After adjusting confounder factors including sex, age, vitamin D levels, HbA1c, ALB, HDLC, eGFR, diabetes microvascular complications and macrovascular, there was an independent association between risk of DMS and age (OR value = 1.160, 95% CI 1.091–1.234, *P* = 0.000), HbA1c(OR value = 1.262, 95% CI 1.046–1.532, *P* = 0.015), and vitamin D deficiency (< 36.2 nmol/L) (OR value = 2.990, 95% CI 1.284–6.964, *P* = 0.011). Our findings suggest that low levels of vitamin D are a predictor of DMS in middle-aged and elderly patients with poor control of type 2 diabetes.

Keywords Vitamin D, Dysmobility syndrome, Type 2 diabetes mellitus, Sarcopenia osteoporosis

Abbreviations

25(OH) Vit D	25-Hydroxyvitamin D
1, 25(OH) $_2$D	1, 25-Hydroxyvitamin D
ALB	Albumin
BMD	Bone mineral density
BMI	Body mass index
DBP	Diastolic pressure
DMS	Dysmobility Syndrome
DXA	Dual-energy X-ray
eGFR	Estimated glomerular filtration rate
ER	Estrogen receptor
FBG	Fasting blood glucose
HbA1c	Glycosylated hemoglobin
HDL-C	High density lipoprotein cholesterol
LDL-C	Low density lipoprotein cholesterol
HGB	Hemoglobin
OP	Osteoporosis
PTH	Parathyroid hormone
SDP	Systolic pressure
T2DM	Type 2 diabetes mellitus

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TC	Cholesterol
TG	Triglyceride
SMI	Skeletal muscle mass index of limbs
uACR	Urine microalbumin/creatinine ratio
VD	Vitamin D
VDR	Vitamin D receptor
WC	Waistline

Type 2 diabetes mellitus (T2DM) is one of the most widespread metabolic diseases, and age represents a risk factor for T2DM. As China gradually enters an aging society, the quality of life of the elderly has attracted people's attention. The literature shows that the probability of DMS in patients with T2DM is significantly higher than that in patients without T2DM[1]. Dysmotility Syndrome(DMS), which was first proposed by the Japanese Orthopaedic Society in 2007[2], includes six conditions: osteoporosis, low muscle mass, low muscle strength, slow gait speed, occurrences of falls in the past year ≥ 1, and obesity, having three or more of these conditions were diagnosed with DMS. Its hazards are an increased risk of falls, fractures, and disability[3], there is a study showing that DMS increases mortality in adults aged 50 and above[4]. There are relevant research reports on each branch of DMS, mainly focusing on the research of bone and muscle as exercise organs, energy metabolism, and endocrine hormone action target organs. Kim et al. found that older adults with diabetes lost approximately 26 percent of muscle mass and approximately 33 percent less muscle strength per year compared with older adults without diabetes[5]. Some literature pointed out that patients with T2DM are prone to combined obesity and increased body fat rate[6], increased incidence of osteoporosis[7], increased incidence of fractures[8], and are prone to problems such as slow gait and balance. However, a new concept, covering multiple factors such as osteoporosis, sarcopenia, balance ability, and obesity, was rarely studied.

Studies have shown that vitamin D levels decline with being older[9] and are associated with diabetes[10]. So patients with T2DM are prone to vitamin D deficiency[11], and some studies show that vitamin D is closely related to obesity[12], osteoporosis[13], and Sarcopenia[14]. Is the level of vitamin D related to the occurrence of DMS in people with T2DM?

At present, the diagnosis of DMS is complex and requires the use of multiple instruments and equipment for measurement, so the diagnosis of DMS requires a higher cost. Therefore we aim to predict the risk of DMS in patients with type 2 diabetes through simple laboratory indicators, such as vitamin D levels, and serum 25-(OH) Vit D can stably and effectively express the level of vitamin D in the body[15].

Materials and methods

Study design

This is a small sample single-center cross-sectional analysis, aimed at providing an effective laboratory predictor of T2DM with DMS. Data comes from the database of hospitalized patients with T2DM in Qinhuangdao First Hospital from October 2020 to February 2022.

Participants

The inclusion criteria included the following: (1) diagnosed with T2DM; (2) over the age of 50; (3) with basic communication, comprehension, and full behavioral skills; (4) without vitamin D supplementation. The exclusion criteria included the following: (1) uncorrected acute complications of diabetes such as diabetic ketoacidosis, hyperosmolar hyperglycemic state; (2) acute cerebrovascular disease, gastrointestinal bleeding, acute and chronic renal failure decompensated, severe liver dysfunction, and other patients with a history of severe physical damage; (3) patients with severe osteoarthritis or neuromuscular disease affecting daily activities; (4) acute infectious disease patients; (5) malignant tumor patients; (6) patients who received vitamin D supplementation; (6) organ failure due to DM macrovascular complications and microvascular complications (eg: Loss of mobility and Visual loss). All patients who met the inclusion criteria signed the informed consent form approved by the Ethics Committee of Qinhuangdao First Hospital and confirmed that all research was performed according to relevant guidelines. The ethical approval number is 2020B004. A total of 330 patients with T2DM were included in this study, 153 males (46.4%) and 177 females (53.6%), According to the 25th percentile of 25-(OH)Vit D (36.2 nmol/L), they were divided into two groups, group A with < 36.2 nmol/L, group B with ≥ 36.2 nmol/L. Patients without DMS were assigned to the Group Non-DMS, and patients with DMS were assigned to the Group DMS.

Variables

Collect the gender, age, history of diabetes and complications, history of hypertension, history of cerebral infarction, history of smoking, and history of drinking from each patient in chronological order. Anthropometric measurements include height, weight, waist circumference (WC), blood pressure, Speed of six meters, and grip strength. Laboratory Examinations: Blood tests were performed after at least 9 h of fasting, and serum 25-(OH) Vit D was measured by using the Abbott Automatic Chemiluminescence Meter. HbA1C, blood uric acid, Serum creatinine, Lipids [total cholesterol (TC), triglyceride (TG), HDL-C, and low-density lipoprotein-cholesterol (LDL-C)], ALB, and Fasting blood glucose (FBG) concentration were measured by direct methods on an automated biochemical analyzer (Hitachi LST008 Tokyo, Japan), and then we calculated the eGFR by using the CKD study equation. Hemoglobin (HGB) was measured by an automatic blood analyzer (XE-2100, Japan).

Diagnosis of DMS

- Osteoporosis: The measured DXA T value of the Lumbar spine or femoral neck ≤ -2.5 was defined as Osteoporosis.
- Slow gait speed: Subjects perform a 6 m walking test at a natural pace, record the time (s), and then calculate that the pace is equal to 6 m/time (s), with ≤ 0.8 m/s as the diagnosis of a slow pace[16].
- Obesity: Body mass index (BMI) was calculated by dividing weight (kg) by height squared (m^2), and BMI ≥ 27 kg/m^2 is defined as obesity[17].
- Low muscle mass: The French MEDILINK bone density instrument was used to measure BMC, lumbar spine L1-4BMD, femoral neck BMD, whole-body muscle content, whole-body fat content, and calculate the skeletal muscle mass index (SMI) = skeletal muscle mass/height 2 (Kg/m^2), low muscle mass was diagnosed by SMI ≤ 5.40 kg/m^2 in women and ≤ 7.0 kg/m^2 in men, which is the diagnostic criteria developed by the Asian sarcopenia working group (ASWG) in 2014[16].
- Low muscle strength: Grip Strength measurement with JAMAR Electronic Grip Dynamometer, The grip strength of the subjects' left and right hands was measured, and the average was taken after three measurements, the average grip strength of both hands is less than 26 kg for men and less than 18 kg for women which is diagnosed as low grip strength[16].
- Occurrences of falls in the past year ≥ 1. Three or more of these conditions were diagnosed with DMS.
- Vitamin D deficiency is defined as a 25(OH)D below 20 ng/ml (50 nmol/liter)[18].

Statistical analysis

The statistical analysis was performed with SPSS version 23.0 (SPSS Inc., Chicago, IL, USA). Measurement data were expressed as mean ± standard deviation, Differences in serum 25(OH)Vit D between Group Non-DMS and Group DMS subjects were evaluated by using a Student's t-test for continuous measures and a chi-square test for categorical measures. Spearman correlation coefficients were determined for bivariate associations of 25(OH) Vit D and other covariates. Binary multivariate logistic regression analysis was done to identify independent factors affecting the risk of T2DM with DMS. We expressed the results of this analysis as odds ratios (ORs) and 95% confidence intervals (CI). $p < 0.05$ was accepted as statistically significant.

Ethics approval and consent to participate

This study had been performed by the Declaration of Helsinki and had been approved by the Ethics Committee of Qinhuangdao First Hospital. Written informed consent statement was obtained from all the participants.

Results

Subsection

Clinical characteristics of the study subjects

The clinical characteristics of the study subjects are shown in Tables 1 and 2. The prevalence of vitamin D deficiency is 67.9%, The detection rate of DMS in patients with T2DM was 25.5% in this study. According to

Variable	Non-DMS group (n = 246)	DMS Group (n = 84)	*t* or χ^2	*P*
Age(years) mean(SD)	64.82(8.16)	73.24(7.47)	− 8.71	< 0.001*
Gender (male/female)	(126/120)	(27/57)	9.16	0.002*
BMI(kg/m^2) mean(SD)	25.30(3.30)	25.54(3.35)	− 0.57	0.571
WC (cm) mean (SD)	91.17(10.15)	94.05(8.33)	− 2.12	0.035*
SBP(mmHg)mean(SD)	144.13(20.16)	142.69(19.50)	0.57	0.570
DBP(mmHg)mean(SD)	84.05(11.26)	80.11(12.19)	2.71	0.007*
History of diabetes(the duration of diabetes)	10.08(8.63)	12.07(9.20)	− 1.80	0.073
Diabetic retinopathy	(202/39)	(71/13)	0.023	0.879
Diabetic neuropathy	(147/94)	(54/30)	0.286	0.593
Diabetic nephropathy	(211/32)	(72/12)	0.067	0.796
coronary artery disease	(190/56)	(59/25)	− 1.23	0.221
Stroke	(203/43)	(67/17)	− 0.56	0.57
Peripheral artery disease	(15/231)	(5/79)	0.08	0.936
History of hypertension	(87/159)	(24/60)	− 1.137	0.256
History of smoking	(192/54)	(69/15)	0.811	0.418
History of drinking	(187/59)	(72/12)	2.059	0.041*

Table 1. Clinical laboratory characteristics of the subjects in different groups. *Means that it is statistically significant. Baseline laboratory values represent the mean ± SD. BMI: body mass index (calculated as weight in kilograms divided by height in meters squared), WC: waist circumference; SBP: systolic blood pressure, DBP: diastolic blood pressure. ACR: a urine random sample.

Variable	Non-DMS group (n = 246)	DMS Group (n = 84)	t or χ^2	P
HbA1c(%)mean(SD)	8.83(4.55)	8.98(2.26)	− 0.28	0.778
FPG(mmol/L)mean(SD)	8.27(3.18)	8.45(3.54)	− 0.418	0.676
25-(OH)Vit D (nmol/L)mean(SD)	47.19(13.01)	41.74(14.60)	3.00	0.003*
TG(mmol/L)mean(SD)	1.90(1.29)	1.94(1.18)	− 0.27	0.785
TC(mmol/L) mean (SD)	5.11(1.48)	5.28(1.38)	− 0.90	0.370
HDL-C(mmol/L)mean (SD)	1.07(0.25)	1.14(0.26)	− 2.17	0.031*
LDL-C(mmol/L) mean (SD)	3.95(18.51)	2.93(1.02)	0.50	0.616
eGFR(ml/min) mean(SD)	95.41(18.71)	84.09(23.76)	3.80	< 0.001*
uACR(mg/mmol)mean(SD)	8.62(31.64)	11.08(21.62)	− 0.612	0.541
ALB(g/L) mean(SD)	43.30(4.95)	41.14(14.60)	3.45	0.001*
HGB(g/L) mean(SD)	140.92(15.66)	132.47(15.15)	4.28	< 0.001*

Table 2. Laboratory characteristics of the subjects in different groups. *Means that it is statistically significant. FPG: fasting plasma glucose, HbA1C: hemoglobin A1C, 25(OH)D: 25-hydroxyvitamin D, TG: triglycerides, TC: cholesterol, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, eGFR: estimated glomerular filtration rate, UACR: urine albumin creatinine ratio, ALB: albumin, HGB: hemoglobin.

research, the DMS group was older than the non-DMS group, the mean age of the DMS group was 73.2 years, 67.9% were women, the mean age of the Non-DMS group was 64.82 years and 48.8% were women. The study notes that vitamin D deficiency was more common in the DMS group (47.19 ± 13.01 nmol/L vs. 41.74 ± 14.60 nmol/L, $p = 0.003$), and the level of vitamin D in male patients was higher and there is a statistical difference (43.38 ± 12.98 vs. 49.59 ± 13.70 $P < 0.05$), In addition, the DMS group have lower DBP(80.11 ± 12.19 vs. 84.05 ± 11.26 $P < 0.05$),eGFR(84.09 ± 23.76 vs. 95.41 ± 18.71 $P < 0.05$), ALB(41.14 ± 14.6 vs. 43.30 ± 4.95 $P < 0.05$), HGB(132.47 ± 15.15 vs. 140.92 ± 15.66 $P < 0.05$). Group DMS is significantly higher in age (73.24 ± 7.47 VS 64.82 ± 8.16 $P < 0.05$), WC (94.05 ± 8.33 VS 91.17 ± 10.15 $P < 0.05$), HDL-C(1.14 ± 0.26 VS 1.07 ± 0.25 $P < 0.05$), and history of diabetes(12.07 ± 9.20 vs. 10.08 ± 8.63 $P < 0.05$). There is currently no statistical difference in BMI, SBP, diabetes complications, FBG, HbA1c, TG, TC, uACR, and LDL-C between the two groups.

Logistic regression analysis of risk factors for DMS in a patient with T2DM

A logistic regression analysis was performed to find the independent factors associated with the risk of DMS in T2DM patients. The dependent variable is group DMS (0 = Non-DMS group,1 = DMS group), The independent variables are respectively gender (0 = female,1 = male), age, diabetic retinopathy(0 = without,1 = with), diabetic neuropathy (0 = without,1 = with), diabetic nephropathy(0 = without,1 = with) and 25-(OH)Vit D (1 = group A, 0 = group B), HbA1c, ALB, HDLC, eGFR were taken as independent variables. The result showed that the T2DM patients with DMS were more likely to relate in the dimensions of age (*OR* value = 1.149, 95%CI 1.091–1.234, $P = 0.000$) and HbA1c(*OR* value = 1.262, 95% CI 1.046–1.523, $P = 0.011$), the level of vitamin D(< 36.2 nmol/L) (*OR* value = 2.990, 95% CI 1.284–6.964, $P = 0.011$) (Table 3).

The dependent variable is group DMS (0 = Non-DMS group, 1 = DMS group), The independent variables are gender(0 = female,1 = male), age, and 25-(OH)Vit D (group A = the level of 25-hydroxyvitamin D < 36.2 nmol/L, group B = the level of 25-hydroxyvitamin D ≥ 36.2 nmol/L), HbA1c, ALB, HDLC, HGB, WC, eGFR,DBP. Backward: conditional was selected.

Discussion

Our study has found that low vitamin D levels were associated with an increased risk of DMS in patients with poorly controlled type 2 diabetes, the proportion of DMS in patients with T2DM was 25.5%. At present, there are few literature reports on the relationship between DMS and DM, and relevant foreign reports mainly focus on osteoporosis[19], muscle strength[20], and gait speed[21]. However, some articles show that people with T2DM can improve their balance and walk after a targeted balance practice program without risk of serious adverse events[22]. And the proportion of vitamin deficiency was 67.9% in patients with T2DM. Previous reports have

Variables	B	Odds Ratio	95% CI	p
Gender(male)	− 0.840	0.432	0.192–0.971	0.042*
Age	0.149	1.160	1.091–1.234	0.000*
25-(OH) Vit D (group A)	1.095	2.990	1.284–6.964	0.011*
HbA1C	0.233	1.262	1.046–1.523	0.015*
WC	0.041	1.042	0.998–1.087	0.060

Table 3. Logistic regression analysis of risk factors for DMS in a patient with T2DM.

also suggested that 80.0% of participants with vitamin D deficiency in Chinese centenarians[23], which indicates that the incidence of vitamin D deficiency increases with age. Vitamin D plays important roles in both skeletal and non-skeletal health, not only acts on bones but also pancreatic beta cells, promoting insulin secretion[24], and reduced serum 25-hydroxyvitamin D [25(OH)D] levels were proven to be significantly associated with sarcopenia in elderly patients with T2DM[25]. Some foreign studies have pointed out that the lack of vitamin D levels can lead to decreased muscle function[26] and increase the risk of reduced bone density, osteoporosis, falls, and fractures[13]. Meta-analysis showed that long-term calcium and vitamin D supplementation significantly reduced total fracture risk by 15% and hip fracture risk by 30%[27], and foreign reports show that timely supplementation of vitamin D can minimize muscle damage[28].

The sources of vitamin D include skin synthesis under sunlight exposure, food, and supplementary additions. Under normal circumstances, the synthesis of vitamin D by B cluster ultraviolet radiation on the skin is the main source (80–90%). Lack of outdoor activities, sunscreen, or clothing to cover exposure to sunlight is an important factor affecting skin vitamin D synthesis. Usually, elderly people reduce their outdoor activities due to poor physical activity and decreased intestinal absorption capacity, which further leads to a deficiency in vitamin D levels.

Meanwhile, our research found that men have higher levels of vitamin D than women, which may be related to male testosterone levels[29]. And the level of HGB in Group DMS is lower. Hemoglobin is a manifestation of human nutritional status, the decline in the nutritional status of elderly patients as aging, and vitamin D deficiency is often associated with anemia[30], which also suggests that vitamin D deficiency can increase the risk of developing DMS.

There are still some deficiencies in this study. First, it is a single-center, monoracial, and small sample study, and people over 80 years old were not selected, which potentially affects the validity of the results. Second, the level of 25-(OH)Vit D in the T2DM population is generally low. Due to the small sample size, a more suitable cut-off point value of vitamin D could not be found. Lastly, the study did not include people who did not have patients with T2DM and could not form an effective comparison. At the same time, it was not observed whether the risk of DMS would decrease after intervention in patients with vitamin D deficiency. A study abroad has shown that there is no evidence yet that Vitamin D supplementation has any positive effect on falls or fracture outcomes[22]. These findings may serve as the basis for intervention trials to reduce the prevalence of DMS.

In summary, the results of this study suggest that the occurrence of DMS is related to a lower level of vitamin D, higher HbA1c, and aging status, and this conclusion needs to be further confirmed through other multicenter studies. At the same time, the diagnosis of DMS is relatively complex and unfriendly to the elderly. Through this study, we learned that vitamin D can be an effective marker for the prevention and treatment of DMS in middle-aged and elderly patients with type 2 diabetes, and this study hopes to recognize the occurrence of DMS earlier by paying attention to vitamin D and blood sugar in patients with type 2 diabetes. Can supplementing with vitamin D reduce the occurrence of DMS, which needs to be further confirmed. Call on more people to know about DMS early, which can improve the quality of life of the elderly.

Conclusion

In our study, Aging status, and level of 25-(OH) Vit D, and HbA1c were identified as key determinants associated with increased risk of DMS in T2DM patients. Prevent the occurrence of DMS early by paying attention to the blood sugar and vitamin D levels of middle-aged and elderly patients with T2DM. Vitamin D level is expected to be a predictor of DMS in middle-aged and elderly patients with type 2 diabetes.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Author contributions

Yongfang Ma: data collection drafting and editing of the paper. Bowei Liu: data analysis and revision of the paper. Fuzai Yin: revision of the paper. Junru Liu: data collection. Xing Wang: data collection. Dongmei Fan: data collection. Lina Sun: data collection. Lanyu Lu: data collection.

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Competing interests

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Additional information

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