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# Early Detection of Mild Cognitive Impairment Using Read Estimation of Vitamin D Levels and Deep Learning in Japanese Elderly: A Pilot Study

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## Abstract

**Background**: Mild cognitive impairment (MCI) is a transitional stage in the trajectory from normal cognition to dementia. Subjects with MCI have a high rate of progression to dementia over a relatively short period, and so there is a great interest in finding good predictors of MCI.

**Methods:** A total of 32 healthy adults age ≥65 years were included in the study, taken from among adult day-care center clients. The serum 25OHD (VitD) values were estimated from baseline demographics datasets (age, sex), anthropometric factors (body mass index (BMI), percent of body fat (%Fat)), VitD intake from a brief self-administered questionnaire on the consumption of fish containing a lot of VitD, eggs and supplements containing VitD, and outdoor exposure history for one week. We then examined the correlation between estimated and serum VitD values. From the baseline demographics datasets, anthropometric factors and estimated VitD, we predicted Mini Mental State Examination (MMSE) scores using the previously reported deep learning framework TensorFlow. The modes of MMSE were decided according to medical criteria using minimal clinically important differences and the range of the correct answers was <3.0. MCI was assumed with MMSE scores of 24-27 and the accuracy of MMSE and MCI were examined.

Results: There was a positive correlation between serum and estimated VitD ($\gamma$=0.937). MMSE and MCI were correctly predicted in 84.7% and 100% of cases, respectively.

**Conclusion:** Our results indicate that deep learning techniques can effectively predict MCI by combining demographics datasets, anthropometric factors, and dietary and lifestyle habits. This system is effective for Japanese people 65 years or older for whom a main source of VitD is assumed to be fish. This algorithm could serve as a tool to aid nurses in clinical decision-making processes for the elderly.

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Deep learning algorithm, Dietary and lifestyle habits, MCI, VitD prediction model

## Introduction

Dementia is a progressive global cognitive impairment syndrome. In 2010, more than 35 million people worldwide were estimated to be living with dementia. Some people with mild cognitive impairment (MCI) will progress to dementia but others remain stable or recover full function [1-2]. MCI is a syndrome characterized by an objective cognitive decline in one or more cognitive domains without any significant impairment in daily-life activities. MCI is a transitional stage in the trajectory from normal cognition to dementia. Subjects with MCI have a high rate of progression to dementia over a relatively short period [3]. Thus, early detection of MCI is an urgent priority for all nations and there is great interest in finding good predictors of MCI. The Mini-Mental State Examination (MMSE) is the best-known and the most often used short screening tool [4]. The optimal diagnostic cutoff point for MCI is reported to be 27 on the MMSE [5].

We previously reported that deep learning techniques can effectively predict MMSE using serum 25OHD (VitD) and baseline demographics datasets (age, sex), anthropometric factors (body mass index (BMI), percent of body fat (%Fat)) in elderly people from 65 to 80 years old [6]. MMSE was correctly predicted in 78.9% of cases, within 3 of the minimum clinically important difference.

Venous blood samples are necessary to determine the serum VitD level, but blood is not easily collected during everyday life. It is reported that it might be possible to predict the VitD status of pregnant Japanese women using a questionnaire of food intake and UV-B radiation [7]. This study aimed to establish a method to easily estimate the VitD level from weekly dietary habits, exposure to sunlight, demographics datasets and anthropometric factors without collecting blood.

Therefore, the present study sought to investigate whether screening for MCI was possible with the easily estimated VitD values using deep learning algorithm.

## Materials & Methods

### Subjects and setting

Prior to conducting this study, approval was obtained from the ethics committee of the Aichi Medical University Ethics Review Board (2017-M052) in Japan. Study researchers were present at the adult day-care centers to ensure the proper management of safety

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and confidentiality in the study. The managers of the adult day-care centers invited clients to participate in the study, and subjects were enrolled from June to August 2023. After obtaining informed consent, we enrolled 32 Japanese men (age: 74.6 ± 7.9) and 102 women (age: 78.5 ± 6.9) in this study.

### Cognitive function test

The Mini Mental State Examination (MMSE) was used to assess cognitive function. It consists of five downstream items of orientation, memory, attention and calculations, language and visual construction. The maximum score on the MMSE is 30 points, and the cutoff score for dementia is 23 to 24 points [8]. Tests were performed by verbal questioning of 5- to 10-min duration by skilled occupational and physical therapists.

### Anthropometric factors

Percent body fat (%Fat) and weight were measured using Inbody 430 (Inbody Japan, Tokyo). Height was measured using InLab (Inbody Japan, Tokyo). BMI was calculated as the weight in kg divided by height in meters squared (kg/m$^2$).

### Serum 25OHD assay

Blood was collected by venipuncture and serum 25OHD (VitD) concentration was measured by Kyoto Biken Laboratories Inc. (Kyoto, Japan), Nikken Igaku Co. (Fukui, Japan) and Falco Holdings Co. (Kyoto, Japan).

### Serum VitD estimation

The serum VitD values were estimated using age, sex, BMI, %Fat and a brief self-administered questionnaire on consumption of seafood containing a lot of VitD and outdoor exposure history [9]. The frequencies of the 9 items, of VitD supplements, multi-vitamins, small fish edible on the bone, dried fish, fatty fish, lean fish, eggs, outdoor exposure history with light clothing and use of sunscreen, were 0, 1-2, 3-4, 5-6 and 7 days/week. The frequencies of 0, 1-2, 3-4, 5-6 and 7 days per a week in the answers on the questionnaire were assigned score of 0, 1, 2, 3, 4 and 5 points, respectively. The kind of fish used in this study were taken in the order of larger consumption in two-or-more-person households in 2022 [10]. The VitD content per 100 g of the small fish with edible bones (11.0 μg) and dried fish (3.0 μg) were assumed from dried sardines and dried horse mackerel, respectively. The representative VitD content per 100 g of fatty fish (10.8 μg) and lean fish (13.7 μg) was estimated from the weighting ratio of taste, yellowtail and saury, tuna, sea bream and salmon, respectively. The VitD intake from fish were calculated from the above representative values and portion sizes. The weighting ratio and portion size were from survey of the JPHC study [11]. The VitD content of VitD supplements and multivitamins were assumed to be 5 and 2.5 μg/day, respectively. The influence of the UV was assumed from the frequency of the sunscreen use and the frequency of outdoor exposure history with light clothing.

### MMSE estimation using deep learning algorithms

We tested the suitability of the deep learning framework TensorFlow (prediction system) [6]. From age, sex, BMI, %Fat and serum VitD, we predicted MMSE with more than 70% accuracy. In this study, MMSE was estimated using estimated VitD instead of measured VitD.

### Criterion for evaluation

The mode of MMSE was decided according to medical criteria using minimal clinically important difference, and the range of correct answers was <3.0.

## Results and Discussion

### Study subjects

The characteristics of the study subjects are shown in Table 1. Obesity was defined as a BMI of ≥25.0 kg/m$^2$. The prevalence of obesity determined by BMI was 21.4-28.0 kg/m$^2$. Thus, it was similar to the mean for all 65-74-year-old Japanese (21.5-24.9 kg/m$^2$).

| Age | No. of participants (% male) | BMI | %Fat | VitD |
|---|---|---|---|---|
| 76.0 ± 5.5 | 32 (12.5) | 23.3 ± 3.8 | 30.4 ± 8.4 | 21.5 ± 6.1 |

Table 1: Characteristics of study subjects (mean ± SD).

### Serum VitD estimation

Serum VitD was estimated from the scores on the questionnaire about VitD intake from supplements and fish consumption containing a lot of VitD and syntheses by UV, %Fat, BMI and sex (Figure 1). There was a positive correlation between serum and estimated VitD ($r$ = 0.943).

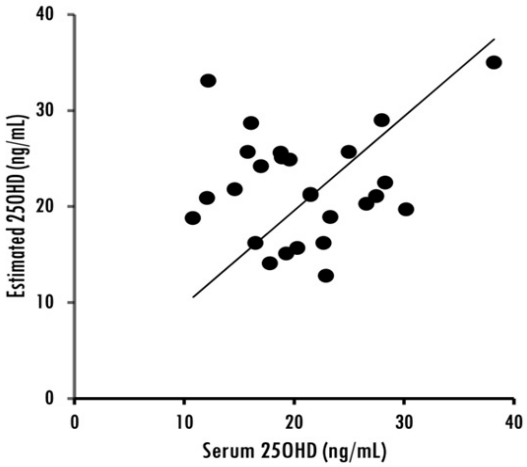


Figure 1: Regression of estimated VitD on serum VitD.

Sarcopenia is a muscle disease (muscle failure) rooted in adverse muscle changes that accrue across a lifetime and is common among adults of older age [12]. Low VitD has been associated with a risk of developing sarcopenia [13, 14]. This estimation system is useful for early detection of sarcopenia in healthy adults age ≥ 65 years.

### MMSE estimation and MCI detection

We applied machine learning and deep learning algorithms to predict MMSE using estimated VitD instead of serum VitD. MMSE and MCI (MMSE 24-27) was correctly predicted in 84.7% and 100.0% of cases, respectively. Dementia is more commonly detected in elderly, and there has been an increase in the use of various treatments over the past 20 years. MCI may be associated with a variety of underlying causes, including Alzheimer's pathophysiology [15]. Our method may

possibly be used to easily predict MCI. On the other hand, there are limitations to this study. We did not examine dairy products as the source of VitD. This algorithm is effective for elderly over 65 years old elderly who live mainly on fish.

Although we only included a small number of cases, the level of inaccuracy with the algorithm was satisfactory for the prediction task. Thus, our findings should be able to serve as a foundation for larger prospective studies.

## Conclusions

Our results indicate that by combining demographics datasets, anthropometric factors, and dietary and lifestyle habits, deep learning techniques can effectively predict MCI. This algorithm could serve as a tool to aid nurses in the clinical decision-making processes for patients over 65 years old.

## Competing Interests

The authors declare that they have no competing interests.

## Author Contributions

Dr. Hasegawa was responsible for the study conception, design, interpretation of data, and drafting of the manuscript.

Dr. Tsuchiya was responsible for the machine learning approach and checking the manuscript.

Dr. Kobayashi was responsible for assessment of VitD intake and checking the manuscript.

Dr. Tsubouchi was responsible for MMSE data acquisition and checking the manuscript.

Ms. Ohta was responsible for data acquisition and checking the manuscript.

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