Associations of circulating vitamin D concentration with physical fitness and cardiometabolic risk factors

血中ビタミン D 濃度と心肺体力および心血管代謝リスクとの関係

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Background (Chapter 1)

Vitamin D has been known to play an important role in bone and mineral homeostasis. High vitamin D status, as assessed by serum 25-hydroxyvitamin D (25(OH)D) concentration, has been recently associated with improved cardiometabolic risk, suggesting that vitamin D may help to reduce the risk of cardiometabolic diseases. However, the causal relationship between vitamin D and cardiometabolic risk reported by randomized controlled intervention studies was unclear in generally healthy adults. Furthermore, physical fitness and body fat are defined as independent and important predictors of cardiometabolic diseases, and closely related with serum 25(OH)D concentration. Thus, it is needed and important to clarify whether there is a direct relationship between serum 25(OH)D concentration and cardiometabolic risk. Therefore, the purpose of the present study was to investigate the relationship between serum 25(OH)D and cardiometabolic risk with consideration of physical fitness and body fat.

Associations between 25(OH)D concentration and lipid profiles: a cross sectional study (Chapter 2)

The purpose of this chapter is to evaluate the associations between serum 25(OH)D and lipid profiles with consideration of visceral fat area (VFA) and cardiorespiratory fitness (CRF). A total of 136 men (age range 20–79 years) participated in our study. Fasting blood samples were analyzed for 25(OH)D, oxidized low-density lipoprotein, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), apolipoprotein (Apo)A-1, and ApoB. VFA was determined by magnetic resonance imaging (MRI) and CRF was assessed by measuring peak oxygen uptake (VO2 peak). The median of 25(OH)D concentration was 35.6 nmol/L, and the prevalence rate of 25(OH)D deficiency was 78.7%. Multiple linear regression analysis revealed that serum 25(OH)D concentration was inversely related to the ratio of LDL-C/HDL-C, TG, ApoB, and the ratio of ApoB/ApoA-1, even after adjustment for VFA and CRF. In conclusion, the present study suggests that serum 25(OH)D is inversely correlated with risk factors of lipid metabolism, such as LDL-C/HDL-C, TG, ApoB, and ApoB/ApoA-1 in Japanese men, and independent of VFA and CRF.

Effects of the interaction between 25(OH)D concentration, cardiorespiratory fitness on glucose profiles: a cross sectional study (Chapter 3)

The purpose of this chapter is to investigate the independent and combined associations of serum 25(OH)D and CRF with the glucose metabolism. Fasting blood samples of 107 men aged 40–79 years were analyzed for 25(OH)D, glucose, insulin, glycated hemoglobin (HbA1c), and lipid profiles. Homeostasis model assessment of insulin resistance index (HOMA-IR) was calculated from the fasting concentrations of
glucose and insulin. VFA was determined by magnetic resonance imaging and CRF by measuring maximal oxygen uptake. Median 25(OH)D concentration was 36.3 nmol/L, while the prevalence of 25(OH)D deficiency was 74.8%. Participants with high CRF had significantly lower HOMA-IR, HbA1c, and insulin values than participants with low CRF (p < 0.05). Higher 25(OH)D concentration was strongly correlated with lower HOMA-IR and insulin values independent of VFA (p < 0.01) but significantly affected by CRF. In the high CRF group, participants with higher 25(OH)D concentration had lower HOMA-IR values than participants with low 25(OH)D concentration (p < 0.05).

Higher 25(OH)D and CRF are crucial for reducing insulin resistance regardless of abdominal fat. Higher 25(OH)D concentration may strengthen the effect of CRF on reducing insulin resistance in middle-aged and elderly Japanese men with high CRF.

**Effects of 1-year vitamin D supplementation on cardiometabolic risk: a double-blind, randomized, placebo-controlled trial (Chapter 4)**

In order to investigate the causal relationship between 25(OH)D concentration and cardiometabolic risk, a 1 year vitamin D supplementation was studied. The participants randomly received daily either 420 IU vitamin D$_3$ or placebo in a double-blind manner for 1 year. Insulin level, glucose level, lipid profiles and inflammatory markers were assessed at baseline and at the end of the study. HOMA-IR was calculated from the fasting glucose and insulin concentrations. VFA and physical activity were also investigated. We found that serum 25(OH)D concentration was significantly increased by approximately 28 nmol/L after one year vitamin D supplementation. After vitamin D supplementation, fasting blood glucose levels and HOMA-IR values significantly decreased (P < 0.01) in the vitamin D supplementation group respectively, and the results are independent of changes in physical activity and visceral fat accumulation. No changes were observed in lipid profiles, inflammatory markers, VFA and physical activity after the 1 year intervention. The results suggests that increasing serum 25(OH)D concentration can improve glucose homeostasis, and is independent of physical activity and visceral fat accumulation.

**Conclusion (chapter 5)**

The present studies revealed that increasing circulating 25(OH)D concentration could improve cardiometabolic risk, especially glucose metabolism, independently of visceral fat and physical fitness levels. Our data suggest that improving circulating vitamin D status maybe effective in the prevention of cardiometabolic diseases in Japanese adults.