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Plasma vitamin D is associated with fasting insulin and homeostatic model assessment of insulin resistance in young adult males, but not females, of the Jerusalem Perinatal Study

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Abstract

Objective: To examine cross-sectional relationships between plasma vitamin D and cardiometabolic risk factors in young adults.

Design: Data were collected from interviews, physical examinations and biomarker measurements. Total plasma 25-hydroxyvitamin D (25(OH)D) was measured using LC–tandem MS. Associations between 25(OH)D and cardiometabolic risk factors were modelled using weighted linear regression with robust estimates of standard errors.

Setting: Individuals born in Jerusalem during 1974–1976.

Subjects: Participants of the Jerusalem Perinatal Study (n 1204) interviewed and examined at age 32 years. Participants were oversampled for low and high birth weight and for maternal pre-pregnancy obesity.

Results: Mean total 25(OH)D concentration among participants was 21·7 (SD 8·9) ng/ml. Among males, 25(OH)D was associated with homeostatic model assessment of insulin resistance (natural log-transformed, $\beta = -0{\cdot}011$, $P = 0{\cdot}004$) after adjustment for BMI. However, these associations were not present among females (P for sex interaction = 0·005).

Conclusions: We found evidence for inverse associations of 25(OH)D with markers of insulin resistance among males, but not females, in a healthy, young adult Caucasian population. Prospective studies and studies conducted on other populations investigating sex-specific effects of vitamin D on cardiometabolic risk factors are warranted.

Keywords
Vitamin D
Cardiometabolic risk
HOMA-IR

Vitamin D receptors are ubiquitous in the body[1], indicating widespread effects of vitamin D in health and disease. Adverse effects of vitamin D deficiency, defined by low circulating concentrations of 25-hydroxyvitamin D (25(OH)D), on bone health have long been known[2]. More recently, potential associations of vitamin D with other chronic diseases, including cancer, CVD, autoimmune disease and type 2 diabetes (T2D), have been demonstrated[3]. For instance, prospective cohort studies have found associations between baseline low circulating 25(OH)D concentrations and incident myocardial infarction, stroke and all-cause mortality[4–6]. However, findings from randomized clinical trials of vitamin D supplementation to reduce hypertension and cardiovascular mortality were inconsistent[7], suggesting more complex relationships between vitamin D and cardiovascular risk development.

A clear understanding of relationships between vitamin D and known cardiometabolic risk factors (CMR), such as fasting blood glucose and related parameters, blood pressure (BP) and lipid levels, as well as the role of potential confounders or mediators, such as obesity, is lacking, particularly among young adults free from overt disease. Further, sex-specific differences have not been fully explored, although it is recognized that men tend to

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have higher 25(OH)D levels than women[8] while having an earlier age of onset of CMR development[9].

We examined cross-sectional relationships between circulating 25(OH)D and CMR among young adult participants of a longitudinal birth cohort study, the Jerusalem Perinatal Study (JPS). We also evaluated whether these relationships differ by sex or are confounded by current BMI.

Methods

Overall setting and study population

The JPS was conducted among women who gave birth as residents of Jerusalem between 1974 and 1976 and who were interviewed within 2 d postpartum (*n* 17 003). The JPS Family Follow-Up study (JPS-1), conducted between 2007 and 2009, was a study designed to determine maternal and offspring genetic risk factors that account for associations between maternal obesity and adulthood CMR among the offspring. The JPS-1 study population consisted of mother–offspring dyads identified and recruited using a stratified sampling of term, singleton live births from the original JPS cohort. Participants were oversampled for low (≤2500 g) and high (≥4000 g) birth weight and for maternal obesity (pre-pregnancy BMI ≥ 27 kg/m^2). Mother–offspring dyads with offspring who had congenital disorders at birth were excluded.

The current study was conducted among offspring JPS-1 participants, 32 (SD 1·3) years old on average. Individuals who self-reported taking medication to lower BP (*n* 13), lipids (*n* 14) or to treat diabetes (*n* 5) were excluded from the analyses. Individuals with a fasting time before blood draw of less than 8 h (*n* 97), fasting glucose outside the range 60–126 mg/dl (*n* 135) or TAG higher than 600 mg/dl (*n* 58) were excluded. The final analytic study population consisted of 1204 offspring (609 males and 595 females). Study procedures were approved by the Institutional Review Boards of the University of Washington, in Seattle, and the Hebrew University Hadassah Medical Center in Jerusalem. All participants provided informed consent.

Data collection

Data collection procedures have been published previously[10]. Briefly, data on anthropomorphic measurements, lifestyle and sociodemographic characteristics were collected during offspring interviews conducted between 2007 and 2009. BMI was calculated as weight (kg) divided by squared height (m^2). BP was measured as the average of three consecutive measurements performed after sitting for 5 min (Omron M7 automated sphygmomanometer). Fasting blood samples were taken using standard procedures. Plasma glucose, HDL-cholesterol (HDL-C) and TAG were measured on the VITROS 5,1FS Chemistry System (Ortho Clinical Diagnostics, Raritan, NJ, USA). Plasma insulin levels were determined using RIA with the Human Insulin-Specific RIA Kit (Millipore, Billerica, MA, USA). Plasma vitamin D (25(OH)D) was measured using LC–tandem MS at the Nutrition and Obesity Research Center, University of Washington (Seattle, WA, USA). The sum of 25(OH)D_2 and 25(OH)D_3 was used in analyses to represent total plasma vitamin D levels.

Statistical analyses

We examined participant characteristics in the entire study cohort and stratified by sex. Means and standard deviations were calculated for continuous variables; numbers and percentages for categorical variables. We used weighted multiple linear regression models to examine associations between offspring 25(OH)D and CMR (BMI, waist circumference, waist:hip ratio, fasting glucose, fasting insulin, homeostatic model assessment of insulin resistance (HOMA-IR), lipids and BP). Ninety-five per cent confidence intervals and *P* values were calculated using robust standard errors. BMI, TAG, LDL-cholesterol (LDL-C) and HDL-C were natural log-transformed to improve model fit. We first examined the relationships among the entire study population with sex as a covariate and an adjustment for multiple testing (critical *P* value $\alpha = 0{\cdot}0045$). Then, we used an interaction term between sex and 25(OH)D to evaluate statistical interaction (at the $P = 0{\cdot}05$ level) between vitamin D and sex on CMR.

We fit two models to evaluate the associations. Model 1 included season of blood draw (December–February, March–May, June–August, September–November) and additional covariates for smoking status (current, former and never), alcohol abstinence (yes/no), intense physical activity participation (yes/no), employment status (yes/no), religiosity (ultra-orthodox, religious and traditionalist/secular/other), ethnic origin (Israel, Morocco, Other Africa, Iraq, Iran, Kurdistan, Yemen, Other Asia and Ashkenazi) and parental history of relevant disease (see below) as confounders and/or to increase precision. The models for fasting blood glucose, insulin and HOMA-IR were adjusted for parental history of diabetes. The models for LDL-C, HDL-C and TAG were adjusted for parental history of heart disease, stroke or elevated cholesterol. The models for systolic and diastolic BP were adjusted for parental history of high BP and stroke. In Model 2, we adjusted for Model 1 variables and BMI, except for the model evaluating BMI as an outcome. The aim of Model 2 was to assess the extent to which BMI mediates or confounds observed associations.

Analyses were performed using the statistical software package Stata v11·0.

Results

Selected characteristics of the study participants are shown in Table 1. Mean total 25(OH)D level was 21·7, 22·9 and 20·5 mmol/l among all participants, males and females, respectively. Overall, 44 % of participants, 36 % of males

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Table 1 Characteristics of the study participants by sex and quartile of plasma vitamin D; offspring (*n* 1204) in the Jerusalem Perinatal Study (JPS; 1974–1976), interviewed and examined at age 32 years in the JPS Family Follow-Up study (JPS-1; 2007–2009)

							Quartile of plasma vitamin D (ng/ml)							
	Total†		Males		Females		1 (<15·4)		2 (15·4–21·4)		3 (21·5–27·4)		4 (>27·4)	
	n or Mean	% or SD	*n* or Mean	% or SD	*n* or Mean	% or SD	*n* or Mean	% or SD	*n* or Mean	% or SD	*n* or Mean	% or SD	*n* or Mean	% or SD
n	1204	–	609	–	595	–	301	–	306	–	288	–	294	–
Plasma 25(OH)D (ng/ml)	21·7	8·9	22·9	8·4	20·5	9·2	11·2	2·9	18·4	1·8	24·3	1·8	33·5	5·8
Females (*n*, %)	595	49·4	–	–	–	–	211	61·3	184	52·9	138	41·0	145	42·2
Males (*n*, %)	609	50·6	–	–	–	–	133	38·7	164	47·1	199	59·1	199	57·9
BMI (kg/m^2)	26·4	5·1	26·8	8·9	26·0	5·6	27·2	5·8	27·0	5·8	26·4	4·4	25·0	3·8
Fasting blood glucose (mg/dl)	80·3	9·0	82·3	8·9	78·3	8·6	80·8	9·0	80·4	9·0	80·8	9·3	79·4	8·8
TAG (mg/dl)	103·3	61·6	116·0	69·2	90·2	49·6	102·0	65·0	105·6	61·9	107·7	65·4	99·2	53·8
LDL-C (mg/dl)	112·2	28·4	117·2	28·3	107·2	27·6	110·4	27·8	111·8	27·4	115·2	30·6	111·4	27·9
HDL-C (mg/dl)	49·9	14·5	43·5	11·1	56·4	14·8	51·2	15·1	48·8	13·9	48·8	14·4	50·4	14·2
Systolic BP (mmHg)	106·4	12·3	113·8	10·4	98·8	9·2	105·5	11·9	107·0	12·7	107·8	12·5	105·4	12·0
Diastolic BP (mmHg)	71·6	8·5	74·7	7·9	68·5	7·8	71·9	8·9	72·2	8·5	72·2	8·3	70·4	8·1
Fasting insulin (μIU/ml)	12·0	7·2	12·6	7·4	11·5	6·9	13·1	7·8	13·5	8·8	11·4	5·6	10·2	5·4
HOMA-IR	2·4	1·5	2·6	1·6	2·2	1·4	2·6	1·6	2·7	1·8	2·3	1·3	2·0	1·2
Waist circumference (cm)	86·5	13·1	91·1	11·8	81·8	12·6	88·2	14·3	87·7	14·2	86·7	11·7	83·7	11·3
Waist:hip ratio	0·83	0·07	0·87	0·06	0·79	0·06	0·83	0·08	0·83	0·07	0·83	0·07	0·82	0·07
Smoking status (*n*, %)														
Former	161	13·7	90	15·2	71	12·1	39	13·1	37	12·5	42	15·1	41	14·2
Current	313	26·6	210	35·5	103	17·6	51	17·1	66	22·3	93	33·3	97	33·7
Abstain from alcohol (*n*, %)														
Abstain	543	46·0	189	31·8	354	60·4	207	69·5	148	49·8	106	37·7	77	26·6
Physical activity‡ (*n*, %)														
Any	353	29·9	224	37·7	129	22·0	72	24·2	68	22·9	92	32·6	118	40·8
Employment status (*n*, %)														
Employed	978	84·2	521	89·1	547	79·3	203	69·8	245	84·2	252	90·0	266	93·7
Religious orthodoxy (*n*, %)														
Traditionalist, secular or other	737	61·2	380	62·4	357	60·0	101	33·6	183	59·8	208	72·2	233	79·3
Religious	236	19·6	124	20·4	112	18·8	54	17·9	68	22·2	58	20·1	54	18·4
Ultra-orthodox	231	19·2	105	17·2	126	21·2	146	48·5	55	18·0	22	7·6	7	2·4
Blood draw month (*n*, %)														
December–February	333	27·7	164	26·9	169	28·4	156	51·8	91	29·7	56	19·4	29	9·9
March–May	198	16·5	91	14·9	107	18·0	58	19·3	61	19·9	49	17·0	26	8·8
September–November	337	28·0	159	26·1	178	29·9	48	16·0	82	26·8	96	33·3	109	37·1

25(OH)D, 25-hydroxyvitamin D; LDL-C, LDL-cholesterol; HDL-C, HDL-cholesterol; BP, blood pressure; HOMA-IR, homeostatic model assessment of insulin resistance.
†May not sum to total due to missing data.
‡Defined as exercise that brings about laboured breathing, increased pulse rate and sweating, lasting for at least 20 min.

Table 2 Overall associations between plasma 25(OH)D (mmol/l) and cardiometabolic risk factors in young adults; offspring (*n* 1204) in the Jerusalem Perinatal Study (JPS; 1974–1976), interviewed and examined at age 32 years in the JPS Family Follow-Up study (JPS-1; 2007–2009)

	Model 1			Model 2		
	Coefficient	SE	*P* value	Coefficient	SE	*P* value
Glucose (mmol/l)	−0·055	0·056	0·327	−0·041	0·056	0·464
Ln(TAG) (mmol/l)	−0·010	0·004	0·005	−0·007	0·003	0·041
Ln(LDL-C) (mmol/l)	−0·001	0·002	0·488	0·000	0·002	0·836
Ln(HDL-C) (mmol/l)	0·004	0·002	0·010	0·003	0·002	0·104
Systolic BP (mmHg)	−0·081	0·058	0·165	−0·015	0·053	0·773
Diastolic BP (mmHg)	−0·108	0·046	0·020	−0·061	0·043	0·157
Ln(BMI) (kg/m^2)	−0·002	0·001	0·030	−0·002	0·001	0·030
Ln(Insulin) (pmol/l)	−0·007	0·003	0·044*	−0·004	0·003	0·213*
Ln(HOMA-IR)	−0·007	0·003	0·034*	−0·004	0·003	0·174*
Waist circumference (cm)	−0·132	0·069	0·056	−0·003	0·036	0·929
Waist:hip ratio	0·000	0·000	0·196	0·000	0·000	0·700

25(OH)D, 25-hydroxyvitamin D; LDL-C, LDL-cholesterol; HDL-C, HDL-cholesterol; BP, blood pressure; HOMA-IR, homeostatic model assessment of insulin resistance.
Model 1 adjusted for season of blood draw, sex, smoking status, alcohol abstinence, religious orthodoxy, physical activity, employment status, ethnic origin and parental history of disease.
Model 2 adjusted for Model 2 covariates, plus BMI.
**P* value for 25(OH)D–sex interaction less than 0·05.

Table 3 Associations between plasma 25(OH)D (mmol/l) and cardiometabolic risk factors among adult females; offspring (*n* 595) in the Jerusalem Perinatal Study (JPS; 1974–1976), interviewed and examined at age 32 years in the JPS Family Follow-Up study (JPS-1; 2007–2009)

	Model 1			Model 2		
	Coefficient	SE	*P* value	Coefficient	SE	*P* value
Glucose (mmol/l)	−0·016	0·065	0·801	−0·003	0·065	0·963
Ln(TAG) (mmol/l)	−0·005	0·004	0·148	−0·002	0·003	0·544
Ln(LDL-C) (mmol/l)	−0·001	0·002	0·599	0·000	0·002	0·901
Ln(HDL-C) (mmol/l)	0·003	0·002	0·193	0·001	0·002	0·606
Systolic BP (mmHg)	−0·126	0·063	0·045	−0·055	0·060	0·362
Diastolic BP (mmHg)	−0·071	0·053	0·180	−0·021	0·051	0·678
Ln(BMI) (kg/m^2)	−0·003	0·001	0·038	−0·003	0·001	0·038
Ln(Insulin) (pmol/l)	0·000	0·004	0·947	0·003	0·004	0·379
Ln(HOMA-IR)	−0·001	0·004	0·886	0·003	0·004	0·431
Waist circumference (cm)	−0·114	0·090	0·205	0·043	0·049	0·377
Waist:hip ratio	0·000	0·000	0·417	0·000	0·000	0·910

25(OH)D, 25-hydroxyvitamin D; LDL-C, LDL-cholesterol; HDL-C, HDL-cholesterol; BP, blood pressure; HOMA-IR, homeostatic model assessment of insulin resistance.
Model 1 adjusted for season of blood draw, smoking status, alcohol abstinance, religious orthodoxy, physical activity, employment status, ethnic origin and parental history of disease.
Model 2 adjusted for Model 1 covariates, plus BMI.

and 52 % of females, had vitamin D deficiency based on the cut-off of 20 ng/ml[11]. Males had higher BMI, fasting blood glucose, TAG, LDL-C, systolic BP, diastolic BP and HOMA-IR compared with females. They also had lower HDL-C levels.

Among all study participants (Table 2), the association between 25(OH)D with TAG was nearly statistically significant in Model 1 after adjustment for other confounders ($P > 0{\cdot}0045$ after multiple testing correction). Each 1 mmol/l increase in 25(OH)D was associated with a 1 % decrease in TAG levels ($P = 0{\cdot}005$). However, the association was attenuated and became non-significant after adjustment for current BMI ($P = 0{\cdot}041$). Among females (Table 3), 25(OH)D was not significantly associated with any outcome of interest. Among males (Table 4), 25(OH)D was inversely associated with insulin and HOMA-IR ($P = 0{\cdot}003$ and 0·002, respectively). Associations of 25(OH)D with HOMA-IR persisted even after adjustment for current BMI (*P*-value = 0·004). Significant statistical interactions were observed between 25(OH)D and sex on insulin and HOMA-IR ($P = 0{\cdot}015$ and 0·012, respectively). We did not observe associations between 25(OH)D and fasting glucose level, LDL-C or BP overall, or among either sex.

Discussion

In the current study, we found that associations of total plasma 25(OH)D with fasting insulin concentration and HOMA-IR were present among males but not females. Interactions

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Table 4 Associations between plasma 25(OH)D (mmol/l) and cardiometabolic risk factors among adult males; offspring (*n* 609) in the Jerusalem Perinatal Study (JPS; 1974–1976), interviewed and examined at age 32 years in the JPS Family Follow-Up study (JPS-1; 2007–2009)

	Model 1			Model 2		
	Coefficient	SE	*P* value	Coefficient	SE	*P* value
Glucose (mmol/l)	−0·095	0·071	0·184	−0·080	0·071	0·260
Ln(TAG) (mmol/l)	−0·015	0·005	0·003	−0·012	0·005	0·012
Ln(LDL-C) (mmol/l)	−0·001	0·002	0·615	0·000	0·002	0·853
Ln(HDL-C) (mmol/l)	0·006	0·002	0·006	0·004	0·002	0·033
Systolic BP (mmHg)	−0·031	0·085	0·716	0·028	0·077	0·715
Diastolic BP (mmHg)	−0·148	0·065	0·023	−0·105	0·061	0·083
Ln(BMI) (kg/m^2)	−0·002	0·001	0·195	−0·002	0·001	0·195
Ln(Insulin) (pmol/l)	−0·013	0·004	0·003*	−0·010	0·004	0·006
Ln(HOMA-IR)	−0·014	0·004	0·002*	−0·011	0·004	0·004*
Waist circumference (cm)	−0·151	0·084	0·072	−0·051	0·042	0·224
Waist:hip ratio	−0·001	0·000	0·206	0·000	0·000	0·449

25(OH)D, 25-hydroxyvitamin D; LDL-C, LDL-cholesterol; HDL-C, HDL-cholesterol; BP, blood pressure; HOMA-IR, homeostatic model assessment of insulin resistance.
Model 1 adjusted for season of blood draw, smoking status, alcohol abstinance, religious orthodoxy, physical activity, employment status, ethnic origin and parental history of disease.
Model 2 adjusted for Model 1 covariates, plus BMI.
**P* value less than 0·0045 (multiple-testing corrected).

between sex and vitamin D on insulin and HOMA-IR were statistically significant. Among males, the association between fasting insulin concentration and 25(OH)D was attenuated after adjustment for BMI, such that it no longer met our stringent criteria for statistical significance.

The inverse association between 25(OH)D and TAG has been widely reported, although many studies report significant associations after adjustment for measures of adiposity, such as BMI[12]. In one such study by Kayaniyil *et al.*, the relationship was attenuated with the addition of BMI to the model but remained statistically significant in their slightly older, more obese and sicker population[13]. It is therefore possible that the relationship between 25(OH)D and TAG is stronger and less subject to attenuation by adiposity among individuals with diagnosed metabolic syndrome, potentially explaining the differences between our study and that by Kayaniyil *et al.*

Evidence for direct effects of vitamin D on TAG levels is still conflicting[12]. Only one randomized controlled trial has reported a significant decrease in TAG levels after vitamin D supplementation[14], while four other randomized controlled trials have failed to duplicate these findings[15–18], including one with both a larger sample size and a larger dose of vitamin D[15]. While indirect effects via vitamin D's influence on intestinal Ca absorption are not thought to cause substantial changes in serum TAG[19], it is plausible that vitamin D reduces serum TAG by suppressing pituitary hormone levels[20] or through its posited effects on glucose metabolism[21], but these hypotheses require further study.

Our analysis of 25(OH)D and concurrently measured fasting insulin in the JPS offspring population found an inverse association between vitamin D and fasting insulin in males, but not females. To confirm these findings in less constrained models, we also examined models using splines and categories of vitamin D insufficiency and insulin resistance (results not shown), but these models did not add anything to our report. Two other studies have examined these sex-specific associations[22,23] and reported associations in females as well as in males. The study by Delvin *et al.* examined French-Canadian adolescents who were 9, 13 and 16 years old during the study[23]. Due to the age difference, results from that study of adolescents and our study on JPS adults, approximately 32 years old, may not be directly comparable. In their study, Yin *et al.* excluded individuals who used vitamin D supplements, smoked or engaged in strenuous exercise, besides individuals excluded for other reasons. Furthermore, only 25 % of their study participants were female[22]. While we adjusted for most of these factors in our study, study population differences, such as diet or genetics, may account for differences in findings from these studies compared with the current study. Other large, population-based studies have also found inverse associations between measures of vitamin D and fasting insulin[24–27] in both sexes; however, these studies did not evaluate sex-specific relationships.

We examined a vitamin D–sex interaction due to the literature supporting sex differences in vitamin D levels[8] and cardiometabolic outcomes[9]. Despite differences between the results of the current analysis and previous studies[22,23,28], some potential reasons supporting observed associations of 25(OH)D levels with fasting insulin and HOMA-IR among males, but not females, exist. Among non-diabetics, insulin resistance is higher among males than females[29]. Middle-aged males have been shown to have a higher risk of incident T2D compared with middle-aged females[25,30,31]. Therefore, if indeed low vitamin D levels contribute to the pathogenesis of T2D, our analysis of 32-year-olds might be expected to show a

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stronger relationship in males than females, who are not expected to develop disease until later.

A prospective cohort study among non-diabetic participants found that lower concentration of baseline 25(OH)D is associated with higher fasting insulin and HOMA-IR, along with other indicators of impaired glucose metabolism[32]. However, they were unable to study incident T2D due to a small number of cases. Conversely, a study by Mattila *et al.* reported that the association of 25(OH)D concentration with incident T2D was attenuated by the addition of concurrent BMI into the model, although the trend of increasing T2D diagnosis with decreasing quartile of serum 25(OH)D remained[33]. Unfortunately, they did not examine markers of insulin resistance and so these two studies are not directly comparable with ours. A randomized controlled trial of vitamin D supplementation found that supplemented, obese, non-diabetic African-American adolescents had improved fasting insulin and HOMA-IR compared with placebo after 6 months[34], indicating that statistically significant improvements may take some time to be observable even in high-risk populations.

At the population level, most cross-sectional studies of 25(OH)D and insulin sensitivity have found associations between the two[35]. However, other cross-sectional studies have found that insulin sensitivity is independent of 25(OH)D in specific populations, such as African Americans[36,37] and the morbidly obese[38]. Beyond the associations between vitamin D and adiposity, evidence from basic science research points to mechanisms for potential associations between vitamin D and glucose homeostasis at the cellular level. Vitamin D receptors[39] and 1α-hydroxylase[40] are expressed on insulin-producing pancreatic β cells. The promoter of the human insulin gene has a vitamin D response element[41], while 1,25-dihydroxy-vitamin D activates transcription of that gene[42]. Evidence has also been found in animal studies. A study in mice found that lack of a functional vitamin D response impaired insulin response[43]. In an *in vivo* rat study, vitamin D deficiency impaired glucose-mediated insulin secretion, which was restored by supplementation[44].

Intervention studies of vitamin D supplementation have not found an association between supplementation and hepatic insulin sensitivity nor with direct measures of insulin sensitivity[35]. Some of these inconsistencies may be related to sex-specific or population-level differences in the relationships.

The major strength of the present study is the data on lifestyle characteristics, demographics and CMR in young adult offspring. That our analyses specifically examine sex-specific differences as well as the role of obesity in these relationships are additional strengths. By examining these relationships in a young, healthy population, we have fewer confounding factors and co-morbidities to consider. However, limitations of our study deserve mention. Levels of 25(OH)D and CMR were measured cross-sectionally and so the temporal relationship of observed associations remains unclear. We tested associations with eleven different CMR outcomes, leading to a substantial correction for multiple testing. Finally, specific characteristics of the study population (e.g. lifestyle and dietary characteristics) may limit generalizability of our findings. Similarities of our findings, particularly overall findings, with previous reports mitigate this concern.

Conclusion

In conclusion, we report that an inverse association of 25(OH)D with TAG is attenuated after adjustment by current BMI in young adults. We also report that 25(OH)D is associated with insulin sensitivity markers in young adult males, but not females. Inconsistencies that are observed, particularly in relation to sex-specific differences and the absence of similar associations in intervention studies, indicate that the relationship between vitamin D and insulin sensitivity may be more complex than anticipated. It would be interesting to conduct follow-up studies in this and similar populations as the participants age. Better understanding of these relationships may help direct future research for public health or clinical applications. Finally, well-designed randomized controlled trials of vitamin D supplementation and CMR are needed in well-defined at-risk populations to determine the utility of vitamin D supplementation in preventing cardiometabolic disease.

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