PECULIARITIES IN THE VITAMIN D – HOMOCYSTEINE – LIVER AXIS IN MEN AS POTENTIAL CONTRIBUTORS TO THE HIGHER PREVALENCE OF METABOLIC DYSFUNCTION - ASSOCIATED FATTY LIVER DISEASE

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BACKGROUND

Homocysteine (Hcy) elevation and vitamin D deficiency have emerged as potential markers of renal and coronary artery disease. Vitamin D enhances the mRNA and protein expression of methionine synthase, thereby lowering the risk of hyperhomocysteinemia.

PURPOSE

An impact of vitamin D on the onset of metabolic dysfunction-associated fatty liver disease (MAFLD) has also been observed, with MAFLD being more frequently present in men.

METHODS

Hcy, 25-hydroxyvitamin D (25(OH)D), vitamin B12, lipids, renal function parameters, and several other diabetes-related markers, including the lipid accumulation product (LAP), a novel biomarker of central lipid accumulation related to the risk of cardiovascular disease, and MAFLD were tested in type 2 diabetic patients (type 2 DM), separately for women and men.
LAP was calculated using the formula:
male LAP = [waist (cm) − 65] × TG concentration (mmol/l) and female LAP = [waist (cm) − 58] × TG concentration (mmol/l).

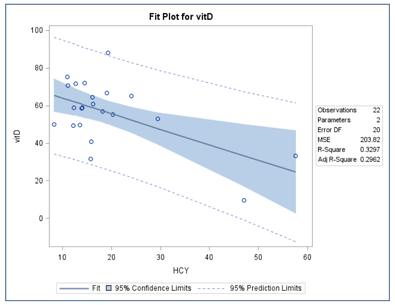
RESULTS

A negative correlation was determined between 25(OH)D and Hcy. In women this correlation is statically significant (rw=-0.574, p=0.005; rm=-0.085, p=0.565). A negative correlation was also determined in women between 25(OH)D and LAP (rw=-0.204, p=0.350; rm=-0.324, p=0.0247).
Hcy correlated significantly with eGFR in women (rw=-0.684. p<0.001) and in men (rm=-0.405, p=0.004). An increase in Hcy is associated with decrease in eGFR levels. The correlation between eGFR and 25(OH)D is positive and statistically significant in women (rw=0.427, p=0.042) and in men (rm=0.337, p=0.019).

- There was no statistically significant difference for 25(OH)D (p=0.7148), Hcy (p=0.3748), LAP (p=0.4348) and eGFR (p=0.5389) by gender.

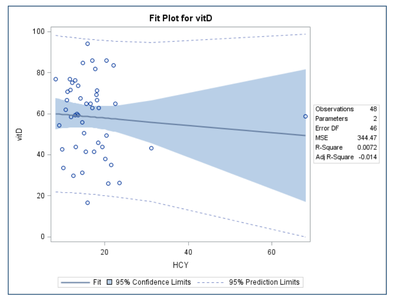
Linear univariate regression

women



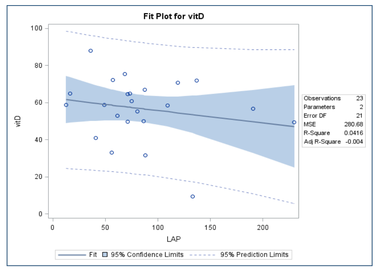
Parameter Estimates					
Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	72.35353	5.92895	12.20	<.0001
HCY	1	-0.83017	0.26469	-3.14	0.0052

men



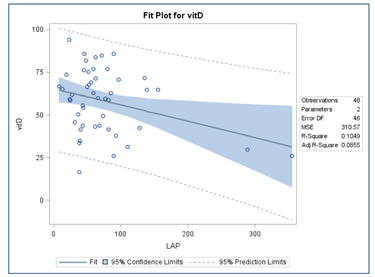
Parameter Estimates					
Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	61.48268	5.91397	10.40	<.0001
HCY	1	-0.17974	0.31056	-0.58	0.5656

women



Parameter Estimates					
Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	62.41646	6.87011	9.09	<.0001
LAP	1	-0.06672	0.06984	-0.96	0.3503

men



Parameter Estimates					
Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	65.40760	3.93639	16.62	<.0001
LAP	1	-0.09565	0.04119	-2.32	0.0247

correlations

women

Simple Statistics			
Variable	N	Mean	Std Dev
vitD	23	56.76	16.72
HCY	22	19.22	11.77
LAP	23	84.70	51.14
GFR	23	87.48	21.66

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0

	HCY	vitD	LAP	GFR
HCY	1.00000	-0.57419	-0.06452	-0.68377
		0.0052	0.7754	0.0005
vitD	-0.57419	1.00000	-0.20408	0.42658
	0.0052		0.3503	0.0424
LAP	-0.06452	-0.20408	1.00000	0.35442
	0.7754	0.3503		0.0970
GFR	-0.68377	0.42658	0.35442	1.00000
	0.0005	0.0424	0.0970	

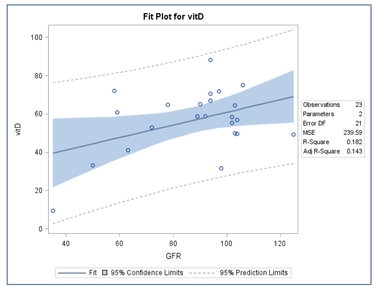
men

Simple Statistics			
Variable	N	Mean	Std Dev
HCY	48	16.98	8.72
vitD	48	58.43	18.43
LAP	48	72.93	62.41
GFR	48	84.16	20.89

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0

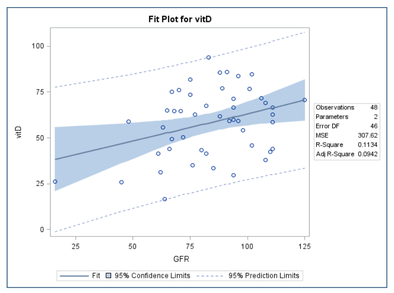
	HCY	vitD	LAP	GFR
HCY	1.00000	-0.08502	0.07663	-0.40520
		0.5656	0.6047	0.0043
vitD	-0.08502	1.00000	-0.32393	0.33679
	0.5656		0.0247	0.0192
LAP	0.07663	-0.32393	1.00000	-0.17260
	0.6047	0.0247		0.2408
GFR	-0.40520	0.33679	-0.17260	1.00000
	0.0043	0.0192	0.2408	

women



Parameter Estimates					
Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	27.96526	13.71044	2.04	0.0542
GFR	1	0.32922	0.15233	2.16	0.0424

men



Parameter Estimates					
Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	33.43245	10.61104	3.15	0.0029
GFR	1	0.29702	0.12243	2.43	0.0192

Univariate linear regression in women pointed at Hcy (R2=0.329) and eGFR (R2=0.182), but not at LAP (R2=0.042) as significant variables in prediction of 25(OH)D levels.
In men eGFR (R2=0.113) and LAP (R2=0.105) were statistically significant in the prediction of 25(OH)D levels, but not Hcy (R2=0.007). This is consistent with the observation about a lack of correlation between Hcy and 25(OH)D in men.

CONCLUSIONS

- In our study, no difference in vitamin D levels was observed between men and women.
- In men there was no significant correlation between vitamin D and Hcy, and vitamin D and LAP.
- Hcy was not among the predictors of vitamin D in men.
- Peculiarities in the vitamin D - Hcy - LAP axis in men compared to women could be among the reasons for the more common onset of MAFLD in men compared to women, with possible explanations involving sex steroids, methionine catabolism, or inflammation.