

Crosstalk between hemostasis inhibitors and cholesterol biomarkers in multiple sclerosis

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SUPPLEMENTARY FILES

Supplementary Table S1. Cholesterol pathway biomarkers and hemostasis inhibitors in HI and MS patients. The mean $\pm$ standard deviations and median (inter-quartile range) are shown in the first and second row, respectively.

Cholesterol Biomarkers	HI	All MS	RR-MS	P-MS
TC, mg/dl	230 $\pm$ 42.5 235 (189 – 259)	234 $\pm$ 40.3 233 (202 – 261)	227 $\pm$ 35.9 224 (199 – 258)	245 $\pm$ 44.8 242 (216 – 270)
HDL, mg/dl	58.3 $\pm$ 16.5 54.5 (48.0 – 63.6)	59.6 $\pm$ 15.3 58.0 (47.5 – 69.0)	59.4 $\pm$ 14.2 57.3 (49.5 – 66.6)	60.0 $\pm$ 17.0 60.5 (46.0 – 72.8)
LDL, mg/dl	141 $\pm$ 35.8 148 (116 – 169)	143 $\pm$ 37.1 140 (117 – 170)	135 $\pm$ 33.9 133 (107 – 162)	155 $\pm$ 39.1 156 (131 – 178)
ApoA-I, mg/dl	167 $\pm$ 35.2 160 (136 – 186)	165 $\pm$ 30.3 162 (142 – 184)	165 $\pm$ 28.0 164 (143 – 183)	163 $\pm$ 33.9 159 (135 – 190)
ApoA-II, mg/dl	40.9 $\pm$ 8.01 40.5 (35.1 – 46.0)	42.1 $\pm$ 7.26 42.0 (37.0 – 46.0)	43.1 $\pm$ 7.17 42.0 (38.0 – 47.3)	40.5 $\pm$ 7.17 39.0 (34.0 – 46.0)
ApoB, mg/dl	102 $\pm$ 26.9 97.3 (85.6 – 113)	103 $\pm$ 25.9 101 (84.0 – 116)	100 $\pm$ 26.3 97.0 (81.6 – 115)	108 $\pm$ 24.7 103 (94.0 – 117)
ApoC-II, mg/dl	4.95 $\pm$ 1.69 4.70 (3.80 – 5.60)	4.93 $\pm$ 1.82 4.70 (3.40 – 6.10)	4.78 $\pm$ 1.87 4.40 (3.38 – 5.70)	5.17 $\pm$ 1.75 5.00 (3.80 – 6.50)
ApoE, mg/dl	5.42 $\pm$ 1.53 5.55 (4.12 – 6.59)	5.82 $\pm$ 1.42 6.03 (5.13 – 6.60)	5.81 $\pm$ 1.48 5.93 (5.11 – 6.60)	5.84 $\pm$ 1.35 6.05 (5.16 – 6.78)
Hemostasis Biomarkers				
HCII, ng/ml	17.5 $\pm$ 12.4 13.8 (8.08 – 23.9)	18.8 $\pm$ 12.3 16.4 (9.90 – 25.0)	18.5 $\pm$ 12.5 16.6 (8.38 – 25.1)	19.4 $\pm$ 12.0 16.2 (12.8 – 25.1)
PAI-1, ng/ml	102 $\pm$ 73.7 84.5 (60.4 – 120)	117 $\pm$ 60.8 103 (79.2 – 145)	112 $\pm$ 46.9 106 (76.3 – 144)	125 $\pm$ 78.0 97.2 (80.9 – 146)
PC, μ g/ml	2.45 $\pm$ 1.35 2.32 (1.43 – 2.77)	2.63 $\pm$ 1.23 2.45 (1.94 – 3.10)	2.60 $\pm$ 1.45 2.25 (1.87 – 2.96)	2.66 $\pm$ 0.794 2.50 (2.12 – 3.25)
PS, μ g/ml	31.4 $\pm$ 6.37 30.0 (26.7 – 34.8)	31.2 $\pm$ 7.04 30.5 (26.9 – 35.0)	30.6 $\pm$ 7.85 30.5 (25.2 – 35.1)	32.1 $\pm$ 5.51 30.5 (27.6 – 34.7)
ADAMTS13, ng/ml	1680 $\pm$ 554 1710 (1290 – 2100)	1560 $\pm$ 505 1520 (1230 – 1789)	1570 $\pm$ 498 1520 (1250 – 1780)	1550 $\pm$ 520 1510 (1180 – 1850)
TM, ng/ml	7.78 $\pm$ 2.70 7.50 (6.15 – 9.00)	7.40 $\pm$ 2.33 7.50 (5.80 – 8.30)	7.06 $\pm$ 2.31 7.05 (5.58 – 8.20)	7.94 $\pm$ 2.30 7.60 (6.95 – 9.25)

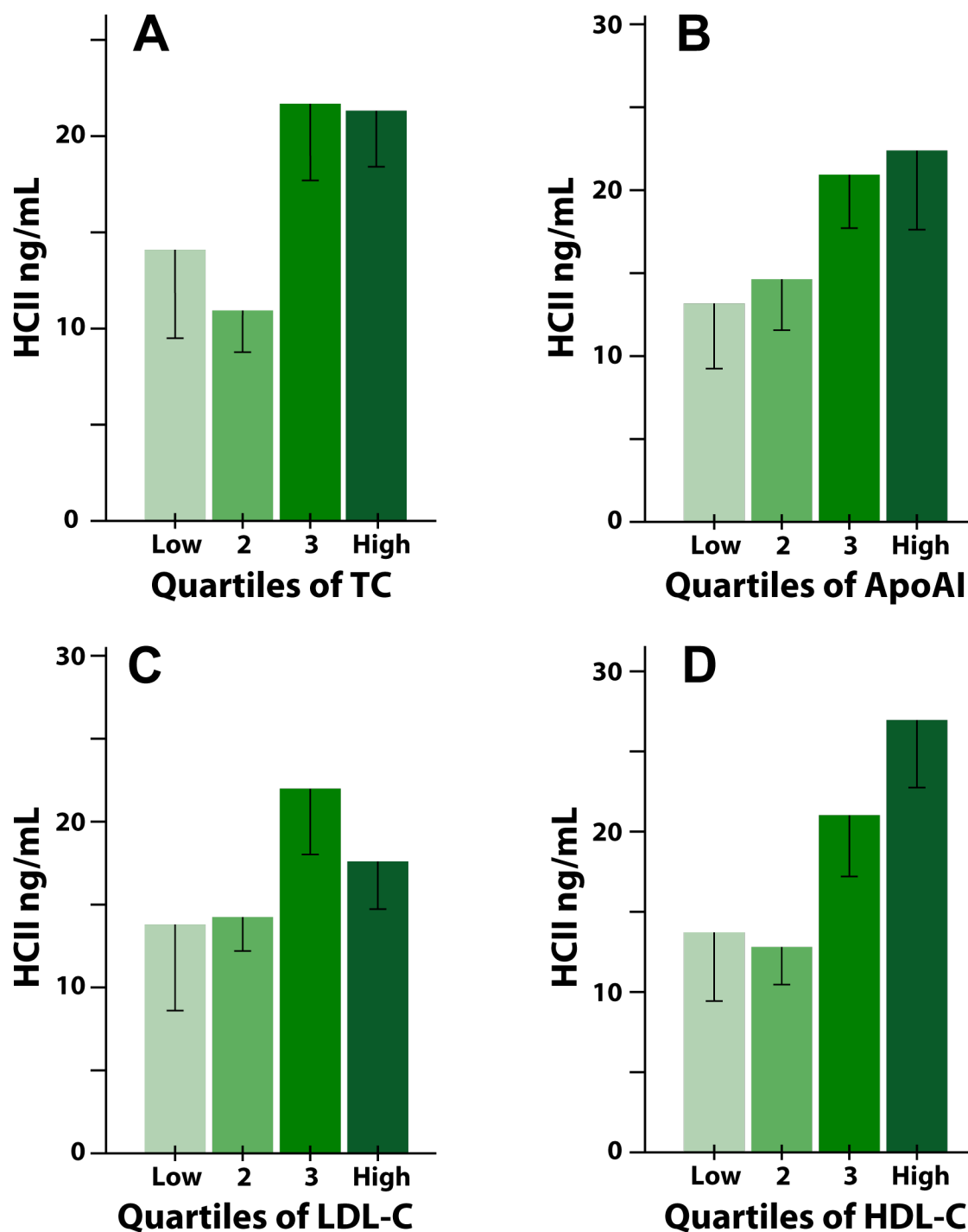
Abbreviations: HCII, Heparin co-factor II; PAI-1, Plasminogen activator inhibitor-1; PC, Protein C; PS, Protein S; TC, Total Cholesterol; HDL, High-Density Lipoprotein; LDL, Low-density Lipoprotein; ApoA-I, Apolipoprotein A-I; ApoA-II, Apolipoprotein A-II; ApoB, Apolipoprotein B; ApoC-II, Apolipoprotein C-II; ApoE, Apolipoprotein E; IQR, Interquartile Range; RR-MS, Relapsing-Remitting MS, P-MS, Progressive MS.

Supplementary Table S2. Associations between hemostasis biomarkers and cholesterol biomarkers in healthy individuals (HI). The partial correlation (r_p) and p -values from multiple linear regression are shown.

	HCII	PAI-1	PC	PS	ADAMTS13	TM
TC	0.058 (0.75)	-0.044 (0.81)	0.16 (0.40)	-0.018 (0.93)	0.085 (0.64)	-0.19 (0.30)
HDL-C	0.28 (0.12)	-0.016 (0.93)	0.22 (0.21)	-0.002 (0.99)	-0.054 (0.76)	-0.048 (0.79)
LDL-C	0.025 (0.89)	-0.11 (0.56)	-0.017 (0.93)	-0.041 (0.83)	0.079 (0.67)	-0.13 (0.48)
ApoA-I	0.052 (0.77)	-0.11 (0.54)	0.20 (0.27)	-0.074 (0.69)	-0.083 (0.64)	-0.073 (0.68)
ApoA-II	-0.17 (0.35)	0.13 (0.48)	0.20 (0.27)	0.15 (0.42)	-0.063 (0.72)	-0.29 (0.10)
Apo B	-0.11 (0.52)	0.12 (0.51)	-0.075 (0.67)	-0.086 (0.64)	0.25 (0.15)	-0.13 (0.46)
ApoC-II	-0.060 (0.74)	-0.11 (0.52)	0.066 (0.71)	0.053 (0.78)	-0.16 (0.37)	-0.13 (0.48)
ApoE	0.35 (0.042) *	-0.001 (1.0)	0.044 (0.80)	0.18 (0.33)	0.018 (0.92)	0.053 (0.77)

The partial correlation (r_p) and p values for the cholesterol biomarker from multiple linear regression analyses are shown for log transformed values FXII, HCII, PAI-1, PC, PS, ADAMTS13, and TM. The multiple linear regression analyses are adjusted for age, gender, body mass index, type of MS (RR vs PMS). The p -values for each cholesterol level that were significant after performing bootstrap analyses are marked with an asterisk.

Supplementary Figure S1. Dependence of heparin cofactor II (HCII) plasma concentrations on cholesterol pathway biomarker level quartiles in healthy individuals (HI). Fig S1A: HCII levels in the lowest, 2nd, 3rd, and highest quartiles of total cholesterol in HI. Fig S1B: HCII levels in the lowest, 2nd, 3rd, and highest quartiles of Apolipoprotein AI (ApoA-I) in HI. Fig S1C: HCII levels in the lowest, 2nd, 3rd, and highest quartiles of low-density lipoprotein cholesterol (LDL-C) in HI. Fig S1D: HCII levels in the lowest, 2nd, 3rd, and highest quartiles of high-density lipoprotein (HDL-C) in HI. The bars represent mean values and the errors bars are standard errors of the mean.



Supplementary Figure S2: Dependence of hemostasis biomarker concentrations on apolipoprotein C-II level quartiles in healthy individuals. Fig S2A: HCII concentration in the lowest, 2nd, 3rd, and highest quartiles of ApoC-II in HI. Fig S2B: PAI-1 concentration in the lowest, 2nd, 3rd, and highest quartiles of ApoC-II in HI Fig S2C: PC concentrations in the lowest, 2nd, 3rd, and highest quartiles of ApoC-II in HI. The bars represent mean values and the errors bars are standard errors of the mean.

