ONLINE-ONLY SUPPLEMENTARY MATERIAL

Supplementary Table 1. Associations between plasma ceramide concentrations and the angiographic severity of coronary stenosis in the LAD artery, _after excluding_ patients with acute ST-elevation myocardial infarction (STEMI).

Linear Regression Analyses	Standard β coefficient(s)	_P_ value
Adjusted model 1		
Cer(d18:1/16:0) (1-SD increment, i.e. 0.10 umol/L)	0.003	0.97
Age (years)	0.089	0.27
Sex (male vs. female)	0.044	0.60
Adjusted model 2		
Cer(d18:1/16:0) (1-SD increment, i.e. 0.10 umol/L)	0.038	0.67
Age (years)	0.072	0.45
Sex (male vs. female)	0.025	0.78
Smoking history (yes vs. no)	0.009	0.91
Prior history of CAD (yes vs. no)	0.178	0.06
Pre-existing diabetes (yes vs. no)	0.008	0.92
Hypertension (yes vs. no)	-0.04	0.64
Dyslipidemia (yes vs. no)	0.082	0.36
hs-CRP (mg/L)	0.01	0.88
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	-0.02	0.79
Adjusted model 1		
Cer(d18:1/18:0) (1-SD increment, i.e. 0.06 umol/L)	0.100	0.23
Age (years)	0.079	0.33
Sex (male vs. female)	0.067	0.42
Adjusted model 2		
Cer(d18:1/18:0) (1-SD increment, i.e. 0.06 umol/L)	0.154	0.08
Age (years)	0.063	0.50
Sex (male vs. female)	0.040	0.64
Smoking history (yes vs. no)	0.014	0.86
Prior history of CAD (yes vs no)	0.200	**0.031**
Pre-existing diabetes (yes. vs no)	0.008	0.92
Hypertension (yes vs. no)	-0.05	0.56
Dyslipidemia (yes vs. no)	0.090	0.30
hs-CRP (mg/L)	-0.01	0.86
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	-0.02	0.83
Adjusted model 1		
Cer(d18:1/20:0) (1-SD increment, i.e. 0.04 umol/L)	0.156	0.06
Age (years)	0.080	0.32
Sex (male vs. female)	0.078	0.35
Adjusted model 2		
Cer(d18:1/20:0) (1-SD increment, i.e. 0.04 umol/L)	0.213	**0.024**
Age (years)	0.065	0.48

Sex (male vs. female)	0.044	0.62
Smoking history (yes vs. no)	0.007	0.93
Prior history of CAD (yes vs. no)	0.220	**0.023**
Pre-existing diabetes (yes vs. no)	0.004	0.67
Hypertension (yes vs. no)	-0.06	0.51
Dyslipidemia (yes vs. no)	0.071	0.41
hs-CRP (mg/L)	-0.02	0.78
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	0.003	0.97
Adjusted model 1		
Cer(d18:1/22:0) (1-SD increment, i.e. 0.29 umol/L)	0.190	**0.020**
Age (years)	0.124	0.13
Sex (male vs. female)	0.080	0.33
Adjusted model 2		
Cer(d18:1/22:0) (1-SD increment, i.e. 0.29 umol/L)	0.283	**0.002***
Age (years)	0.104	0.26
Sex (male vs. females)	0.044	0.61
Smoking history (yes vs. no)	0.023	0.77
Prior history of CAD (yes vs. no)	0.259	**0.006**
Pre-existing diabetes (yes vs. no)	0.053	0.54
Hypertension (yes vs. no)	-0.03	0.73
Dyslipidemia (yes vs. no)	0.053	0.54
hs-CRP (mg/L)	-0.05	0.58
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	-0.01	0.87
Adjusted model 1		
Cer(d18:1/24:0) (1-SD increment, i.e. 1.15 umol/L)	0.172	**0.040**
Age (years)	0.126	0.13
Sex (male vs. female)	0.065	0.42
Adjusted model 2		
Cer(d18:1/24:0) (1-SD increment, i.e. 1.15 umol/L)	0.254	**0.005***
Age (years)	0.103	0.27
Sex (male vs. female)	0.023	0.79
Smoking history (yes vs. no)	0.024	0.77
Prior history of CAD (yes vs. no)	0.248	**0.005**
Pre-existing diabetes (yes vs. no)	0.067	0.45
Hypertension (yes vs. no)	-0.03	0.77
Dyslipidemia (yes vs. no)	0.035	0.69
hs-CRP (mg/L)	-0.028	0.74
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	-0.02	0.78
Adjusted model 1		
Cer(d18:1/24:1) (1-SD increment, i.e. 0.37 umol/L)	0.086	0.31
Age (years)	0.075	0.37
Sex (male vs. female)	0.064	0.44
Adjusted model 2		

Cer(d18:1/24:1) (1-SD increment, i.e. 0.37 umol/L)	0.127	0.16
Age (years)	0.049	0.60
Sex (male vs. female)	0.038	0.67
Smoking history (yes vs. no)	0.023	0.79
Prior history of CAD (yes vs. no)	0.187	**0.040**
Pre-existing diabetes (yes vs. no)	0.008	0.93
Hypertension (yes vs. no)	-0.04	0.66
Dyslipidemia (yes vs. no)	0.090	0.31
hs-CRP (mg/L)	-0.01	0.88
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	-0.02	0.83

Sample size, n=152 after excluding patients with acute STEMI (n=15). Data are expressed as standardized beta coefficients as tested by linear regression analysis. Severity of LAD stenosis (included as a continuous measure and logarithmically transformed) was the dependent variable in all multivariable linear regression models. Each plasma ceramide was expressed per 1-SD increment. For clarity, the significant p-values are highlighted in bold.

NB: Hypertension was defined as blood pressure ≥140/90 mmHg or drug treatment; pre-existing diabetes was defined as self-reported physician-diagnosed diabetes, or use of glucose-lowering medications); dyslipidemia was defined as LDL-cholesterol ≥2.6 mmol/L or drug treatment.

*Adjusted model 2: these associations remained statistically significant even after adjustment for multiplicity by using the Benjamini-Hochberg step-up procedure (with a FDR of 0.05).

Supplementary Table 2. Associations between plasma ceramide concentrations and presence of LAD stenosis ≥50%, _after excluding_ patients with acute ST-elevation myocardial infarction.

Logistic Regression Analyses	Odds Ratio (95% CI)	_P_ value
Adjusted model 1		
Cer(d18:1/16:0) (1-SD increment, i.e. 0.10 umol/L)	1.16 (0.82-1.05)	0.40
Age (years)	1.01 (0.98-1.05)	0.42
Sex (male vs. female)	1.54 (0.71-3.34)	0.27
Adjusted model 2		
Cer(d18:1/16:0) (1-SD increment, i.e. 0.10 umol/L)	1.22 (0.84-1.79)	0.29
Age (years)	1.01 (0.98-1.05)	0.46
Sex (male vs. female)	1.44 (0.63-3.29)	0.38
Smoking history (yes vs. no)	0.99 (0.60-1.62)	0.97
Prior history of CAD (yes vs. no)	2.07 (0.94-4.56)	0.07
Pre-existing diabetes (yes vs. no)	1.35 (0.54-3.33)	0.52
Hypertension (yes vs. no)	0.58 (0.22-1.47)	0.25
Dyslipidemia (yes vs. no)	1.25 (0.46-3.39)	0.66
hs-CRP (mg/L)	1.00 (0.99-1.02)	0.71
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	0.99 (0.98-1.01)	0.57
Adjusted model 1		
Cer(d18:1/18:0) (1-SD increment, i.e. 0.06 umol/L)	1.28 (0.88-1.86)	0.19
Age (years)	1.01 (0.98-1.04)	0.48
Sex (male vs. female)	1.58 (0.73-3.39)	0.24
Adjusted model 2		
Cer(d18:1/18:0) (1-SD increment, i.e. 0.06 umol/L)	1.36 (0.92-2.02)	0.13
Age (years)	1.01 (0.98-1.05)	0.47
Sex (male vs. female)	1.45 (0.64-3.31)	0.38
Smoking history (yes vs. no)	1.00 (0.61-1.64)	0.99
Prior history of CAD (yes vs. no)	2.15 (0.98-4.74)	0.06
Pre-existing diabetes (yes vs. no)	1.32 (0.54-3.27)	0.54
Hypertension (yes vs. no)	0.53 (0.20-1.36)	0.19
Dyslipidemia (yes vs. no)	1.29 (0.47-3.53)	0.62
hs-CRP (mg/L)	1.00 (0.99-1.02)	0.85
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	0.99 (0.98-1.01)	0.67
Adjusted model 1		
Cer(d18:1/20:0) (1-SD increment, i.e 0.04 umol/L)	1.37 (0.96-1.94)	0.08
Age (years)	1.01 (0.98-1.04)	0.48
Sex (male vs. female)	1.62 (0.76-3.46)	0.22
Adjusted model 2		
Cer(d18:1/20:0) (1-SD increment, i.e 0.04 umol/L)	1.49 (1.03-2.17)	**0.035**
Age (years)	1.01 (0.98-1.05)	0.47
Sex (male vs. female)	1.45 (0.64-3.32)	0.37
Smoking history (yes vs. no)	0.98 (0.59-1.61)	0.93
Prior history of CAD (yes vs. no)	2.33 (1.05-5.20)	**0.010**

Pre-existing diabetes (yes vs. no)	1.52 (0.61-3.83)	0.37
Hypertension (yes vs. no)	0.50 (0.19-1.31)	0.37
Dyslipidemia (yes vs. no)	1.18 (0.43-3.25)	0.75
hs-CRP (mg/L)	1.00 (0.98-1.02)	0.91
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	0.99 (0.98-1.01)	0.71
Adjusted model 1		
Cer(d18:1/22:0) (1-SD increment, i.e. 0.29 umol/L)	1.45 (1.02-2.07)	**0.041**
Age (years)	1.02 (0.99-1.05)	0.24
Sex (male vs. female)	1.63 (0.76-3.48)	0.21
Adjusted model 2		
Cer(d18:1/22:0) (1-SD increment, i.e. 0.29 umol/L)	1.70 (1.14-2.54)	**0.010***
Age (years)	1.02 (0.98-1.06)	0.28
Sex (male vs. female)	1.43 (0.63-3.29)	0.39
Smoking history (yes vs. no)	1.02 (0.62-1.69)	0.94
Prior history of CAD (yes vs. no)	2.73 (1.19-6.28)	**0.019**
Pre-existing diabetes (yes vs. no)	1.63 (0.64-4.13)	0.30
Hypertension (yes vs. no)	0.55 (0.21-1.46)	0.23
Dyslipidemia (yes vs. no)	1.08 (0.38-3.00)	0.88
hs-CRP (mg/L)	0.99 (0.98-1.02)	0.93
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	0.99 (0.98-1.01)	0.62
Adjusted model 1		
Cer(d18:1/24:0) (1-SD increment, i.e. 1.15 umol/L)	1.41 (1.00-2.00)	**0.05**
Age (years)	1.02 (0.99-1.06)	0.23
Sex (male vs. female)	1.52 (0.72-3.22)	0.27
Adjusted model 2		
Cer(d18:1/24:0) (1-SD increment, i.e. 1.15 umol/L)	1.66 (1.11-2.49)	**0.013***
Age (years)	1.02 (0.98-1.06)	0.26
Sex (male vs. female)	1.32 (0.58-3.01)	0.50
Smoking history (yes vs. no)	1.03 (0.62-1.70)	0.92
Prior history of CAD (yes vs. no)	2.67 (1.16-6.11)	**0.020**
Pre-existing diabetes (yes vs. no)	1.76 (0.69-4.49)	0.24
Hypertension (yes vs. no)	0.56 (0.21-1.49)	0.25
Dyslipidemia (yes vs. no)	0.97 (0.34-2.74)	0.94
hs-CRP (mg/L)	1.00 (0.98-1.02)	0.93
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	0.99 (0.98-1.01)	0.54
Adjusted model 1		
Cer(d18:1/24:1) (1-SD increment, i.e. 0.37 umol/L)	1.21 (0.86-1.71)	0.27
Age (years)	1.01 (0.97-1.04)	0.54
Sex (male vs. female)	1.53 (0.72-3.25)	0.27
Adjusted model 2		
Cer(d18:1/24:1) (1-SD increment, i.e. 0.37 umol/L)	1.26 (0.86-1.82)	0.23
Age (years)	1.01 (0.97-1.05)	0.56
Sex (male vs. female)	1.39 (0.62-3.15)	0.42

Smoking history (yes vs. no)	1.03 (0.62-1.68)	0.92
Prior history of CAD (yes vs. no)	2.04 (0.93-4.45)	0.07
Pre-existing diabetes (yes vs. no)	1.33 (0.54-3.28)	0.54
Hypertension (yes vs. no)	0.56 (0.21-1.43)	0.22
Dyslipidemia (yes vs. no)	1.30 (0.48-3.54)	0.60
hs-CRP (mg/L)	1.00 (0.98-1.02)	0.80
e-GFR$_{MDRD}$ (mL/min/1.73 m^2)	0.99 (0.98-1.01)	0.56

Sample size, n=152 after excluding patients with acute STEMI (n=15). Data are expressed as odds ratio and 95% confidence intervals (CI) as tested by univariable and multivariable logistic regression analysis. The presence of LAD stenosis ≥50% was the dependent variable in all multivariable linear regression models. For clarity, the significant p-values are highlighted in bold.

NB: Hypertension was defined as blood pressure ≥140/90 mmHg or drug treatment; pre-existing diabetes was defined as self-reported physician-diagnosed diabetes, or use of glucose-lowering medications); dyslipidemia was defined as LDL-cholesterol ≥2.6 mmol/L or drug treatment.

*Adjusted model 2: these associations remained statistically significant even after adjustment for multiplicity by using the Benjamini-Hochberg step-up procedure (with a FDR of 0.05).

Supplementary Table 3. Associations between plasma ceramide concentrations and the angiographic severity of coronary stenoses as assessed by the Gensini score, _after excluding_ patients with acute ST-elevation myocardial infarction.

Logistic Regression Analyses	Odds Ratio	95% CI	_P_ value
Cer(d18:1/16:0) (1-SD increment, i.e., 0.10 umol/L)			
Adjusted model 1	0.91	0.63 – 1.31	0.62
Adjusted model 2	1.08	0.72 – 1.62	0.69
Cer(d18:1/18:0) (1-SD increment, i.e. 0.06 umol/L)			
Adjusted model 1	1.29	0.86 – 1.93	0.21
Adjusted model 2	1.51	1.00 – 2.42	0.054
Cer(d18:1/20:0) (1-SD increment, i.e. 0.04 umol/L)			
Adjusted model 1	1.28	0.88 – 1.85	0.19
Adjusted model 2	1.56	1.03 – 2.32	**0.034**
Cer(d18:1/22:0) (1-SD increment, i.e. 0.29 umol/L)			
Adjusted model 1	1.18	0.82 – 1.67	0.38
Adjusted model 2	1.57	1.04 – 2.39	**0.031**
Cer(d18:1/24:0) (1-SD increment, i.e. 1.15 umol/L)			
Adjusted model 1	1.16	0.81 – 1.64	0.42
Adjusted model 2	1.54	1.01 – 2.31	**0.047**
Cer(d18:1/24:1) (1-SD increment, i.e., 0.37 umol/L)			
Adjusted model 1	1.13	0.79 – 1.62	0.50
Adjusted model 2	1.32	0.88 – 1.99	0.17

Sample size, n=152 after excluding patients with acute STEMI (n=15). Data are expressed as odds ratio(s) and 95% confidence intervals (CI). The Gensini Score (included as categorical variable, i.e., 1st tertile _vs._ 2nd and 3rd tertiles combined) was the dependent variable in all multivariable logistic regression models. Each plasma ceramide was expressed per 1-SD increment. For clarity, the significant p-values are highlighted in bold.

Other covariates included in multivariable logistic regression models (along with each plasma ceramide) were as follows: model 1: adjusted for age and sex; model 2: additionally adjusted for smoking, prior history of CAD, pre-existing diabetes (defined as self-reported physician-diagnosed diabetes, or use of glucose-lowering medications), hypertension (blood pressure ≥140/90 mmHg or drug treatment), dyslipidemia (LDL-cholesterol ≥2.6 mmol/L or drug treatment), plasma hs-CRP and e-GFR$_{MDRD}$ values.