

Supplemental Material for „Association of Metabolic Phenotypes with Coronary Artery Disease and Cardiovascular Events in Patients with Stable Chest Pain“
Kammerlander et al., Diabetes Care 2020.

Supplemental Table 1. Odds ratios for coronary computed tomography findings according to metabolic phenotypes.

	OR (95% CI)	p-value	adj. OR (95% CI)	p-value
	Crude		Adjusted*	
Severe coronary artery calcification (AS>400)				
<i>All patients</i>				
MHN (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
MHO	0.90 (0.65 – 1.24)	0.520	1.06 (0.75 – 1.49)	0.743
MUN	1.70 (1.42 – 2.04)	<0.001	1.84 (1.39 – 2.44)	<0.001
MUO	1.66 (1.40 – 1.97)	<0.001	2.29 (1.75 – 3.00)	<0.001
<i>Metabolically Unhealthy</i>				
MUN	1.00 (Reference)	---	1.00 (Reference)	---
MUO	0.92 (0.73 – 1.17)	0.501	1.22 (0.94 – 1.58)	0.137
Severe coronary artery disease ($\geq 70\%$ stenosis ‡)				
<i>All patients</i>				
MHN (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
MHO	1.10 (0.74 – 1.63)	0.628	1.22 (0.82 – 1.81)	0.335
MUN	1.64 (1.16 – 2.30)	0.005	1.53 (1.08 – 2.17)	0.017
MUO	1.46 (1.05 – 2.03)	0.025	1.61 (1.15 – 2.17)	0.005
<i>Metabolically Unhealthy</i>				
MUN	1.00 (Reference)	---	1.00 (Reference)	---
MUO	0.89 (0.65 – 1.23)	0.476	1.07 (0.77 – 1.50)	0.674
High-risk plaque				
<i>All patients</i>				
MHN (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
MHO	0.94 (0.79 – 1.12)	0.490	1.04 (0.86 – 1.25)	0.671
MUN	1.47 (1.24 – 1.73)	<0.001	1.39 (1.16 – 1.66)	<0.001
MUO	1.29 (1.10 – 1.50)	0.001	1.44 (1.22 – 1.70)	<0.001
<i>Metabolically Unhealthy</i>				
MUN	1.00 (Reference)	---	1.00 (Reference)	---
MUO	0.88 (0.74 – 1.04)	0.122	1.03 (0.86 – 1.24)	0.735

AS denotes Agatston score; MHN, metabolically healthy non-obese; MHO, metabolically healthy obese; MUN, metabolically unhealthy non-obese; MUO, metabolically unhealthy obese.

* Multivariable model adjusted for age, sex, smoking, and total cholesterol

‡ $\geq 70\%$ stenosis in any segment or $\geq 50\%$ stenosis in the left main artery.

Supplemental Table 2. Odds ratios of body mass index as continuous variable for coronary computed tomography findings.

	OR (95% CI)	p-value	adj. OR (95% CI)	p-value
	Crude		Adjusted*	
Severe coronary artery calcification (AS>400)				
<i>Metabolically Healthy</i>				
BMI (per 1kg/m ² increase)	0.99 (0.96-1.02)	0.440	1.01 (0.98 – 1.04)	0.497
<i>Metabolically Unhealthy</i>				
BMI (per 1kg/m ² increase)	0.99 (0.97-1.01)	0.292	1.01 (0.99 – 1.04)	0.219
Severe coronary artery disease				
<i>Metabolically Healthy</i>				
BMI (per 1kg/m ² increase)	1.01 (0.98-1.04)	0.531	1.02 (0.99 – 1.06)	0.236
<i>Metabolically Unhealthy</i>				
BMI (per 1kg/m ² increase)	0.98 (0.95-1.01)	0.108	1.00 (0.97 – 1.02)	0.722
High-risk plaques				
<i>Metabolically Healthy</i>				
BMI (per 1kg/m ² increase)	0.99 (0.97-1.00)	0.107	1.00 (0.98 – 1.01)	0.858
<i>Metabolically Unhealthy</i>				
BMI (per 1kg/m ² increase)	0.98 (0.97-0.99)	0.006	1.00 (0.98 – 1.01)	0.599

BMI denotes body mass index.

* Multivariable model adjusted for age, sex, smoking, and total cholesterol.

Supplemental Table 3. Odds ratios for coronary computed tomography findings according to metabolic phenotypes.

	adj. OR (95% CI)	p-value	adj. OR (95% CI)	p-value	adj. OR (95% CI)	p-value
	Model A †		Model B ‡		Model C §	
Severe coronary artery calcification (AS>400)						
<i>All patients</i>						
MHN (ref.)	1.00 (Reference)	---	1.00 (Reference)	---	1.00 (Reference)	---
MHO	1.05 (0.74 - 1.48)	0.795	1.09 (0.76 - 1.55)	0.649	1.05 (0.74 - 1.48)	0.802
MUN	1.96 (1.48 - 2.60)	<0.001	1.61 (1.19 - 2.17)	0.002	1.83 (1.38 - 2.42)	<0.001
MUO	2.31 (1.76 - 3.04)	<0.001	2.07 (1.56 - 2.75)	<0.001	2.25 (1.71 - 2.95)	<0.001
<i>Metabolically Unhealthy</i>						
MUN	1.00 (Reference)	---	1.00 (Reference)	---	1.00 (Reference)	---
MUO	1.15 (0.89 - 1.50)	0.292	1.26 (0.97 - 1.64)	0.083	1.21 (0.93 - 1.58)	0.148
Severe coronary artery disease ($\geq 70\%$ stenosis *)						
<i>All patients</i>						
MHN (ref.)	1.00 (Reference)	---	1.00 (Reference)	---	1.00 (Reference)	---
MHO	1.24 (0.83 - 1.85)	0.298	1.25 (0.83 - 1.88)	0.283	1.20 (0.81 - 1.79)	0.368
MUN	1.59 (1.12 - 2.26)	0.010	1.43 (0.99 - 2.06)	0.058	1.52 (1.07 - 2.15)	0.018
MUO	1.63 (1.16 - 2.28)	0.005	1.50 (1.05 - 2.13)	0.024	1.58 (1.12 - 2.21)	0.008
<i>Metabolically Unhealthy</i>						
MUN	1.00 (Reference)	---	1.00 (Reference)	---	1.00 (Reference)	---
MUO	1.06 (0.76 - 1.48)	0.738	1.07 (0.77 - 1.50)	0.685	1.08 (0.77 - 1.50)	0.671
High-risk plaques						
MHN (ref.)	1.00 (Reference)	---	1.00 (Reference)	---	1.00 (Reference)	---
MHO	1.05 (0.87 - 1.26)	0.616	1.08 (0.89 - 1.31)	0.429	1.04 (0.86 - 1.25)	0.682
MUN	1.45 (1.21 - 1.74)	<0.001	1.24 (1.03 - 1.50)	0.024	1.39 (1.16 - 1.66)	<0.001
MUO	1.47 (1.25 - 1.74)	<0.001	1.32 (1.11 - 1.57)	0.002	1.44 (1.22 - 1.71)	<0.001
<i>Metabolically Unhealthy</i>						
MUN	1.00 (Reference)	---	1.00 (Reference)	---	1.00 (Reference)	---
MUO	1.01 (0.84 - 1.21)	0.944	1.05 (0.88 - 1.27)	0.580	1.03 (0.86 - 1.24)	0.735

AS denotes Agatston score; MHN, metabolically healthy non-obese; MHO, metabolically healthy obese; MUN, metabolically unhealthy non-obese; MUO, metabolically unhealthy obese.

* $\geq 70\%$ stenosis in any segment or $\geq 50\%$ stenosis in the left main artery,

† Suppl. Model A: Adjusted for age, sex, smoking, total cholesterol, and race (non-hispanic white vs. others)

‡ Suppl. Model B: Adjusted for age, sex, smoking, total cholesterol, and statin treatment (at baseline)

§ Suppl. Model C: Adjusted for age, sex, smoking, total cholesterol, and sedentary lifestyle

§ Suppl. Model C: Adjusted for age, sex, smoking, and sedentary lifestyle

Supplemental Table 4. Odds ratios for coronary computed tomography findings according to metabolic phenotypes.

	OR (95% CI) Crude	p-value	adj. OR (95% CI)	p-value			
			Adjusted*				
Severe coronary artery calcification (AS>400)							
<i>All patients</i>							
MHN-II (ref.)	1.00 (Reference)	---	1.00 (Reference)	---			
MHO-II	1.13 (0.52 – 2.44)	0.758	1.32 (0.60 – 2.93)	0.493			
MUN-II	1.70 (1.11 – 2.63)	0.015	2.27 (1.44 – 3.57)	<0.001			
MUO-II	1.70 (1.10 – 2.62)	0.016	2.80 (1.78 – 4.43)	<0.001			
<i>Metabolically Unhealthy</i>							
MUN-II	1.00 (Reference)	---	1.00 (Reference)	---			
MUO-II	1.00 (0.82 – 1.21)	0.976	1.23 (1.00 – 1.53)	0.051			
Severe coronary artery disease (≥70% stenosis †)							
<i>All patients</i>							
MHN-II (ref.)	1.00 (Reference)	---	1.00 (Reference)	---			
MHO-II	1.73 (0.73 – 4.05)	0.210	1.87 (0.79 – 4.43)	0.155			
MUN-II	1.48 (0.86 – 2.57)	0.157	1.71 (0.98 – 2.98)	0.058			
MUO-II	1.45 (0.84 – 2.52)	0.181	1.89 (1.09 – 3.30)	0.025			
<i>Metabolically Unhealthy</i>							
MUN-II	1.00 (Reference)	---	1.00 (Reference)	---			
MUO-II	0.98 (0.76 – 1.27)	0.875	1.12 (0.86 – 1.45)	0.418			
High-risk plaque							
<i>All patients</i>							
MHN-II (ref.)	1.00 (Reference)	---	1.00 (Reference)	---			
MHO-II	1.04 (0.69 – 1.58)	0.839	1.12 (0.72 – 1.73)	0.607			
MUN-II	1.18 (0.94 – 1.49)	0.154	1.53 (1.20 – 1.96)	0.001			
MUO-II	1.12 (0.89 – 1.41)	0.335	1.63 (1.27 – 2.08)	<0.001			
<i>Metabolically Unhealthy</i>							
MUN-II	1.00 (Reference)	---	1.00 (Reference)	---			
MUO-II	0.95 (0.84 – 1.07)	0.397	1.06 (0.93 – 1.22)	0.379			

AS denotes Agatston score; MHN, metabolically healthy non-obese; MHO, metabolically healthy obese; MUN, metabolically unhealthy non-obese; MUO, metabolically unhealthy obese.

* Multivariable model adjusted for age, sex, smoking, and total cholesterol.

† ≥70% stenosis in any segment or ≥50% stenosis in the left main artery.

Supplemental Table 5. Predictive value of metabolic phenotypes for the composite endpoint death, nonfatal myocardial infarction, and hospitalization for unstable angina.

	HR (95% CI)	p-value	adj. HR (95% CI)	p-value
	Crude		Adjusted*	
Combined endpoint				
<i>All patients</i>				
MHN (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
MHO	0.98 (0.57 – 1.69)	0.951	1.06 (0.62 – 1.82)	0.834
MUN	1.69 (1.08 – 2.64)	0.022	1.61 (1.02 – 2.53)	0.038
MUO	0.99 (0.61 – 1.60)	0.967	1.06 (0.66 – 1.72)	0.799
<i>Metabolically Unhealthy</i>				
MUN (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
MUO	0.59 (0.37 – 0.93)	0.024	0.67 (0.42 – 1.07)	0.094

MHN denotes metabolically healthy non-obese; MHO, metabolically healthy obese; MUN, metabolically unhealthy non-obese; MUO, metabolically unhealthy obese.

* Multivariable model adjusted for age, sex, smoking, and total cholesterol.

Supplemental Table 6. Hazard ratios of body mass index as continuous variable for the composite endpoint death, nonfatal myocardial infarction, and hospitalization for unstable angina

	HR (95% CI)	p-value	adj. HR (95% CI)	p-value
	Crude		Adjusted*	
Combined Endpoint				
<i>Metabolically Healthy</i>				
BMI (per 1kg/m ² increase)	0.97 (0.92-1.02)	0.178	0.97 (0.92 – 1.03)	0.302
<i>Metabolically Unhealthy</i>				
BMI (per 1kg/m ² increase)	0.98 (0.94-1.02)	0.247	0.99 (0.95 – 1.03)	0.653

BMI denotes body mass index

* Multivariable model adjusted for age, sex, smoking, and total cholesterol

Supplemental Table 7. Predictive value of metabolic phenotypes for the composite endpoint death, nonfatal myocardial infarction, and hospitalization for unstable angina.

	adj. HR (95% CI)	p-value	adj. HR (95% CI)	p-value	adj. HR (95% CI)	p-value						
	Model A *		Model B †		Model C ‡							
Combined endpoint												
<i>All patients</i>												
MHN (ref.)	1.00 (Reference)	---	1.00 (Reference)	---	1.00 (Reference)	---						
MHO	1.06 (0.62-1.83)	0.820	1.07 (0.60-1.90)	0.830	0.98 (0.57-1.69)	0.940						
MUN	1.62 (1.03-2.55)	0.037	1.52 (0.92-2.49)	0.101	1.53 (0.97-2.41)	0.069						
MUO	1.03 (0.64-1.68)	0.891	1.00 (0.60-1.69)	0.987	0.95 (0.59-1.55)	0.851						
<i>Metabolically Unhealthy</i>												
MUN (ref.)	1.00 (Reference)	---	1.00 (Reference)	---	1.00 (Reference)	---						
MUO	0.64 (0.40-1.02)	0.061	0.66 (0.40-1.08)	0.098	0.62 (0.39-0.99)	0.047						

MHN denotes metabolically healthy non-obese; MHO, metabolically healthy obese; MUN, metabolically unhealthy non-obese; MUO, metabolically unhealthy obese

* Suppl. Model A: Adjusted for age, sex, smoking, total cholesterol, and race (non-hispanic white vs. others)

† Suppl. Model B: Adjusted for age, sex, smoking, statin, total cholesterol, and aspirin treatment (at day 60)

‡ Suppl. Model C: Adjusted for age, sex, smoking, total cholesterol, and sedentary lifestyle

Supplemental Table 8. Association of number of metabolic syndrome risk factors with coronary computed tomography findings and the composite endpoint death, nonfatal myocardial infarction, and hospitalization for unstable angina. Results indicate odds ratios (OR) and hazard ratios (HR) respectively.

	OR/HR (95% CI)	p-value	adj. OR/HR (95% CI)	p-value
	Crude		Adjusted*	
Severe coronary artery calcification (AS>400)				
All				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
1 MetS factor	1.08 (0.73 – 1.58)	0.711	1.59 (1.06 – 2.38)	0.026
2 MetS factors	1.94 (1.33 – 2.82)	0.001	2.64 (1.78 – 3.90)	<0.001
3 MetS factors	2.83 (1.88 – 4.26)	<0.001	3.75 (2.43 – 5.79)	<0.001
Non-obese (BMI<30)				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
1 MetS factor	1.18 (0.74 – 1.88)	0.486	1.66 (1.02 – 2.70)	0.042
2 MetS factors	2.05 (1.30 – 3.24)	0.002	2.44 (1.51 – 3.94)	<0.001
3 MetS factors	3.84 (2.21 – 6.68)	<0.001	4.52 (2.51 – 8.15)	<0.001
Obese (BMI ≥30)				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
1 MetS factor	0.90 (0.44 – 1.83)	0.771	1.34 (0.64 – 2.80)	0.436
2 MetS factors	1.73 (0.88 – 3.43)	0.114	2.59 (1.27 – 5.27)	0.009
3 MetS factors	2.27 (1.12 – 4.60)	0.023	2.94 (1.40 – 6.16)	0.004
Severe coronary artery disease (≥70% stenosis				
†)				
All				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
1 risk factor	0.99 (0.62 – 1.57)	0.956	1.21 (0.76 – 1.94)	0.423
2 MetS factors	1.37 (0.87 – 2.15)	0.175	1.59 (1.00 – 2.51)	0.049
3 MetS factors	1.67 (1.01 – 2.78)	0.047	1.95 (1.17 – 3.26)	0.011
Non-obese (BMI<30)				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
1 MetS factor	1.17 (0.65 – 2.11)	0.592	1.35 (0.74 – 2.45)	0.329
2 MetS factors	1.75 (0.97 – 3.13)	0.061	1.90 (1.05 – 3.45)	0.033
3 MetS factors	2.24 (1.08 – 4.64)	0.031	2.55 (1.21 – 5.35)	0.014
Obese (BMI ≥30)				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
1 MetS factor	0.68 (0.32 – 1.44)	0.312	0.88 (0.41 – 1.89)	0.741
2 MetS factors	0.88 (0.42 – 1.83)	0.726	1.09 (0.52 – 2.29)	0.825
3 MetS factors	1.09 (0.50 – 2.35)	0.832	1.21 (0.55 – 2.65)	0.633
High-risk plaque				
All				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---

1 MetS factor	0.94 (0.76 – 1.15)	0.525	1.30 (1.04 – 1.61)	0.021
2 MetS factors	1.28 (1.04 – 1.57)	0.020	1.67 (1.34 – 2.08)	<0.001
3 MetS factors	1.51 (1.18 -1.93)	0.001	1.96 (1.51 – 2.56)	<0.001
<i>Non-obese (BMI<30)</i>				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
1 MetS factor	0.98 (0.77 – 1.25)	0.874	1.37 (1.05 – 1.79)	0.019
2 MetS factors	1.37 (1.06 – 1.77)	0.015	1.70 (1.29 – 2.24)	<0.001
3 MetS factors	1.88 (1.29 – 2.73)	0.001	2.28 (1.53 – 3.41)	<0.001
<i>Obese (BMI ≥30)</i>				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
1 MetS factor	0.86 (0.59 – 1.27)	0.448	1.17 (0.78 – 1.75)	0.458
2 MetS factors	1.17 (0.80 – 1.72)	0.413	1.55 (1.04 – 2.32)	0.032
3 MetS factors	1.34 (0.89 – 2.01)	0.164	1.70 (1.11 – 2.62)	0.015
Combined Endpoint				
All				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
1 MetS factor	0.44 (0.26 – 0.75)	0.003	0.50 (0.29 – 0.86)	0.012
2 MetS factors	0.74 (0.45 – 1.22)	0.242	0.81 (0.49 – 1.34)	0.408
3 MetS factors	0.71 (0.38 – 1.33)	0.279	0.79 (0.42 – 1.49)	0.470
<i>Non-obese (BMI<30)</i>				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
1 MetS factor	0.41 (0.21 – 0.78)	0.007	0.47 (0.24 – 0.92)	0.028
2 MetS factors	0.90 (0.49 – 1.63)	0.721	0.99 (0.54 – 1.81)	0.972
3 MetS factors	1.06 (0.45 – 2.48)	0.888	1.22 (0.52 – 2.86)	0.648
<i>Obese (BMI ≥30)</i>				
0 MetS factors (ref.)	1.00 (Reference)	---	1.00 (Reference)	---
1 MetS factor	0.50 (0.18 – 1.37)	0.178	0.56 (0.20 – 1.55)	0.268
2 MetS factors	0.61 (0.23 – 1.62)	0.321	0.65 (0.24 – 1.72)	0.382
3 MetS factors	0.59 (0.20 – 1.72)	0.334	0.62 (0.21 – 1.80)	0.377

MetS denotes Metabolic Syndrome.

Adjusted for age, sex, smoking, and total cholesterol.