

SUPPLEMENTAL MATERIAL

Supplemental Table I: Multivariable-adjusted Interaction of Muscle Attenuation and Metabolic Risk Factor Association with Age

	Interaction with Age	Age ≤ 49 years		Age > 49 Years	
		Estimate (95% CI)*	p-value	Estimate (95% CI)*	p-value
Continuous Variables					
Glucose	0.9	2.12 (0.93, 3.32)	0.0005	2.32 (1.17, 3.47)	<0.0001
Log HOMA-IR	0.08	0.04 (0.01, 0.07)	0.01	0.03 (-0.00, 0.05)	0.07
Log Triglycerides	0.3	0.08 (0.04, 0.13)	0.0005	0.04 (0.01, 0.07)	0.01
HDL	0.5	-0.08 (-1.29, 1.14)	0.9	-0.67 (-1.43, 0.01)	0.09
SBP	0.6	2.52 (1.46, 3.59)	<0.0001	1.04 (0.14, 1.94)	0.02
DBP	<0.0001	1.44 (0.71, 2.18)	0.0001	0.16 (-0.33, 0.64)	0.5
Dichotomous Variables					
Insulin Resistance	<0.0001	1.49 (1.20, 1.85)	0.0003	1.10 (0.97, 1.25)	0.1
IFG	0.4	1.08 (0.88, 1.34)	0.5	1.22 (1.08, 1.37)	0.001
Diabetes	0.2	2.00 (1.40, 2.88)	0.0002	1.25 (1.08, 1.44)	0.003
Metabolic Syndrome	0.3	1.48 (1.21, 1.80)	0.0001	1.45 (1.28, 1.64)	<0.0001
High Triglycerides	0.8	1.15 (0.94, 1.41)	0.2	1.12 (1.00, 1.26)	0.04
Low HDL	0.2	1.04 (0.86, 1.27)	0.7	0.99 (0.88, 1.11)	0.8
Hypertension	0.02	1.39 (1.12, 1.72)	0.003	1.17 (1.05, 1.32)	0.006

*Estimates of effect size for continuous variables and of odds ratios of the condition for dichotomous variables per 1 standard deviation decrease in muscle attenuation (overall: 6.6) with 95% confidence interval.

Supplemental Table II – Data stratified by cohort, modeled per 1 SD decrease in muscle HU

	Women						Men					
	Overall		Offspring		Gen 3		Overall		Offspring		Gen 3	
	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value	Estimate (95% CI)	p-value
Glucose												
Simple	2.13 (1.28, 2.99)	<.0001	1.96 (0.81, 3.11)	0.0009	2.63 (1.29, 3.97)	0.0001	2.11 (0.76, 3.46)	0.002	3.12 (1.19, 5.05)	0.002	-0.70 (-3.04, 1.65)	0.56
+BMI	1.06 (0.22, 1.90)	0.01	1.01 (-0.12, 2.13)	0.08	1.31 (-0.02, 2.64)	0.05	1.31 (-0.03, 2.65)	0.06	2.16 (0.19, 4.12)	0.03	-1.16 (-3.46, 1.13)	0.32
+VAT (no BMI)	0.12 (-0.75, 0.99)	0.78	-0.17 (-1.34, 1.00)	0.78	0.71 (-0.64, 2.06)	0.30	1.22 (-0.14, 2.59)	0.08	2.27 (0.30, 4.25)	0.03	-1.56 (-3.89, 0.77)	0.19
Log HOMA-IR												
Simple	0.05 (0.02, 0.07)	0.0004	0.05 (0.01, 0.09)	0.01	0.09 (0.05, 0.12)	<.0001	-0.00 (-0.03, 0.03)	0.98	0.02 (-0.02, 0.07)	0.28	-0.01 (-0.05, 0.03)	0.52
+BMI	-0.01 (-0.03, 0.02)	0.61	0.00 (-0.04, 0.04)	0.98	0.02 (-0.01, 0.05)	0.20	-0.04 (-0.06, 0.01)	0.003	-0.03 (-0.07, 0.01)	0.12	-0.04 (-0.07, 0.00)	0.03
+VAT (no BMI)	-0.04 (-0.07, 0.02)	0.0003	-0.04 (-0.08, 0.00)	0.05	-0.02 (-0.04, 0.01)	0.28	-0.06 (-0.08, 0.03)	<.0001	-0.04 (-0.07, 0.00)	0.08	-0.07 (-0.11, 0.04)	<.0001
Log Trig												
Simple	0.09 (0.07, 0.12)	<.0001	0.08 (0.04, 0.12)	0.0001	0.12 (0.08, 0.17)	<.0001	-0.01 (-0.05, 0.02)	0.48	-0.01 (-0.05, 0.04)	0.73	-0.03 (-0.10, 0.04)	0.40
+BMI	0.05 (0.02, 0.08)	0.0003	0.04 (0.01, 0.08)	0.02	0.06 (0.02, 0.11)	0.007	-0.04 (-0.08, 0.01)	0.01	-0.04 (-0.08, 0.01)	0.09	-0.05 (-0.12, 0.02)	0.14
+VAT (no BMI)	0.00 (-0.02, 0.03)	0.79	-0.00 (-0.04, 0.04)	0.86	0.02 (-0.02, 0.07)	0.33	-0.07 (-0.10, 0.03)	0.0002	-0.05 (-0.09, 0.00)	0.05	-0.10 (-0.16, 0.03)	0.004
HDL												
Simple	-1.54 (-2.51, -0.57)	0.002	-0.84 (-1.99, 0.30)	0.15	-1.94 (-3.64, -0.24)	0.03	0.59 (0.17, 1.35)	0.13	0.33 (0.54, 1.20)	0.46	2.54 (0.98, 4.09)	0.001
+BMI	-0.24 (-1.20, 0.71)	0.62	0.04 (-1.09, 1.17)	0.95	0.05 (-1.62, 1.71)	0.96	1.29 (0.56, 2.03)	0.0006	1.08 (0.22, 1.93)	0.01	3.01 (1.53, 4.50)	<.0001
+VAT (no BMI)	0.95 (-0.03, 1.93)	0.06	1.14 (-0.03, 2.30)	0.06	1.03 (-0.65, 2.70)	0.23	1.73 (1.00, 2.46)	<.0001	1.15 (0.30, 2.01)	0.008	3.92 (2.48, 5.36)	<.0001

SBP												
Simple	1.70 (0.76, 2.65)	0.0004	1.36 (0.04, 2.69)	0.04	3.10 (1.66, 4.54)	<.0001	0.97 (0.11, 1.83)	0.03	0.86 (-0.33, 2.06)	0.16	2.16 (0.62, 3.70)	0.006
+BMI	0.71 (-0.23, 1.65)	0.14	0.73 (-0.60, 2.06)	0.28	1.53 (0.11, 2.94)	0.03	0.47 (-0.38, 1.32)	0.28	0.40 (-0.82, 1.62)	0.52	1.90 (0.42, 3.39)	0.01
+VAT (no BMI)	0.05 (-0.94, 1.03)	0.92	0.20 (-1.22, 1.61)	0.79	0.85 (-0.58, 2.29)	0.24	0.31 (-0.55, 1.17)	0.48	0.51 (-0.73, 1.74)	0.42	1.34 (-0.14, 2.82)	0.08
DBP												
Simple	0.58 (0.04, 1.13)	0.04	0.34 (-0.36, 1.03)	0.35	1.50 (0.61, 2.38)	0.001	0.11 (-0.45, 0.67)	0.71	0.31 (-0.39, 1.01)	0.39	0.23 (-0.86, 1.32)	0.68
+BMI	0.03 (-0.52, 0.57)	0.92	0.02 (-0.68, 0.73)	0.95	0.61 (-0.27, 1.49)	0.18	-0.26 (-0.81, 0.30)	0.36	-0.05 (-0.76, 0.66)	0.89	0.06 (-1.00, 1.12)	0.91
+VAT (no BMI)	-0.35 (-0.92, 0.21)	0.22	-0.21 (-0.96, 0.53)	0.58	0.15 (-0.74, 1.04)	0.74	-0.44 (-1.00, 0.12)	0.12	-0.04 (-0.75, 0.67)	0.92	-0.38 (-1.42, 0.67)	0.48
Insulin Resistance												
Simple	1.27 (1.10, 1.47)	0.001	1.10 (0.91, 1.32)	0.32	1.86 (1.42, 2.43)	<.0001	1.05 (0.90, 1.22)	0.56	1.07 (0.89, 1.28)	0.46	1.05 (0.77, 1.43)	0.77
+BMI	0.95 (0.80, 1.14)	0.60	0.83 (0.67, 1.04)	0.11	1.37 (1.02, 1.84)	0.04	0.84 (0.70, 1.02)	0.08	0.84 (0.66, 1.06)	0.14	0.87 (0.61, 1.24)	0.45
+VAT (no BMI)	0.72 (0.59, 0.88)	0.001	0.63 (0.49, 0.82)	0.0005	1.10 (0.79, 1.53)	0.59	0.75 (0.62, 0.90)	0.002	0.82 (0.67, 1.02)	0.08	0.71 (0.49, 1.01)	0.06
IFG												
Simple	1.31 (1.13, 1.50)	0.0002	1.25 (1.06, 1.48)	0.009	1.47 (1.14, 1.89)	0.003	1.05 (0.92, 1.19)	0.49	1.04 (0.90, 1.22)	0.57	1.11 (0.85, 1.45)	0.44
+BMI	1.14 (0.98, 1.32)	0.10	1.13 (0.95, 1.36)	0.16	1.17 (0.87, 1.58)	0.30	0.98 (0.86, 1.12)	0.76	0.99 (0.85, 1.16)	0.90	1.06 (0.81, 1.39)	0.68
+VAT (no BMI)	0.98 (0.83, 1.16)	0.86	1.01 (0.84, 1.23)	0.89	0.99 (0.71, 1.38)	0.96	0.94 (0.82, 1.07)	0.34	0.95 (0.81, 1.12)	0.57	0.98 (0.75, 1.29)	0.90
Diabetes												
Simple	1.34 (1.10, 1.64)	0.004	1.26 (0.99, 1.59)	0.06	1.83 (1.25, 2.67)	0.002	1.26 (1.06, 1.51)	0.009	1.32 (1.09, 1.61)	0.005	0.96 (0.54, 1.72)	0.90
+BMI	1.16 (0.93, 1.45)	0.19	1.10 (0.86, 1.42)	0.45	1.55 (0.95, 2.53)	0.08	1.12 (0.93, 1.35)	0.24	1.18 (0.97, 1.44)	0.10	0.83 (0.45, 1.51)	0.54

+VAT (no BMI)	0.95 (0.74, 1.21)	0.66	0.88 (0.66, 1.17)	0.38	1.44 (0.88, 2.37)	0.15	1.14 (0.94, 1.37)	0.18	1.23 (1.00, 1.51)	0.048	0.79 (0.44, 1.42)	0.44
Metabolic Syndrome												
Simple	1.85 (1.58, 2.15)	<.0001	1.81 (1.49, 2.20)	<.0001	1.97 (1.53, 2.54)	<.0001	1.10 (0.96, 1.26)	0.15	1.14 (0.97, 1.34)	0.10	1.09 (0.82, 1.43)	0.56
+BMI	1.50 (1.27, 1.77)	<.0001	1.56 (1.26, 1.92)	<.0001	1.48 (1.11, 1.97)	0.008	0.89 (0.76, 1.03)	0.12	0.92 (0.77, 1.09)	0.33	0.94 (0.68, 1.28)	0.68
+VAT (no BMI)	1.22 (1.02, 1.45)	0.03	1.29 (1.04, 1.60)	0.02	1.17 (0.84, 1.64)	0.36	0.80 (0.68, 0.94)	0.006	0.92 (0.76, 1.10)	0.34	0.73 (0.53, 1.02)	0.07
High Trig												
Simple	1.40 (1.22, 1.61)	<.0001	1.30 (1.09, 1.54)	0.003	1.60 (1.26, 2.04)	0.0001	0.91 (0.80, 1.03)	0.15	0.94 (0.81, 1.09)	0.40	0.85 (0.66, 1.11)	0.24
+BMI	1.24 (1.07, 1.43)	0.0036	1.19 (1.00, 1.42)	0.045	1.34 (1.03, 1.74)	0.03	0.81 (0.71, 0.94)	0.004	0.84 (0.71, 0.99)	0.04	0.79 (0.60, 1.04)	0.10
+VAT (no BMI)	1.05 (0.89, 1.23)	0.55	1.03 (0.85, 1.24)	0.79	1.13 (0.84, 1.52)	0.42	0.75 (0.65, 0.86)	<.0001	0.82 (0.70, 0.97)	0.02	0.67 (0.51, 0.90)	0.007
Low HDL												
Simple	1.17 (1.02, 1.34)	0.02	1.09 (0.92, 1.30)	0.33	1.30 (1.04, 1.64)	0.02	0.85 (0.74, 0.99)	0.04	0.86 (0.72, 1.02)	0.09	0.72 (0.52, 0.98)	0.04
+BMI	1.01 (0.87, 1.17)	0.87	0.97 (0.80, 1.17)	0.73	1.07 (0.83, 1.38)	0.62	0.75 (0.64, 0.88)	0.0005	0.74 (0.61, 0.90)	0.003	0.65 (0.47, 0.90)	0.009
+VAT (no BMI)	0.86 (0.73, 1.02)	0.08	0.84 (0.68, 1.03)	0.09	0.93 (0.70, 1.23)	0.59	0.70 (0.59, 0.82)	<.0001	0.73 (0.61, 0.89)	0.002	0.56 (0.40, 0.78)	0.0007
Hypertension												
Simple	1.29 (1.12, 1.48)	0.0003	1.25 (1.05, 1.48)	0.01	1.47 (1.16, 1.87)	0.002	1.10 (0.95, 1.26)	0.19	1.07 (0.92, 1.26)	0.38	1.29 (0.95, 1.75)	0.11
+BMI	1.11 (0.96, 1.29)	0.16	1.10 (0.92, 1.31)	0.30	1.21 (0.92, 1.59)	0.17	0.99 (0.86, 1.14)	0.89	0.99 (0.84, 1.16)	0.89	1.19 (0.87, 1.63)	0.28
+VAT (no BMI)	0.98 (0.84, 1.15)	0.85	0.97 (0.80, 1.18)	0.75	1.10 (0.82, 1.47)	0.52	0.95 (0.82, 1.09)	0.46	0.98 (0.83, 1.16)	0.79	1.07 (0.77, 1.47)	0.70

Note: Data presented include effect size expressed per 1 standard deviation decrease in muscle attenuation with 95% confidence intervals.

* All models are adjusted for: age, current smoking status, alcohol use, and physical activity.

Menopausal status and hormone replacement therapy are also included for in models among women.

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Additional covariate in SBP and DBP model: Hypertension Treatment;

Additional covariate in HDL and TG models: Lipid Lowering Treatment;

Additional covariate for FPG: Treatment for Diabetes.

