Markers Of Oxidative Damage Are Not Elevated In Otherwise Healthy Individuals With The Metabolic Syndrome

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ONLINE APPENDIX

Supplemental Table 1. Clinical characteristics, risk components of metabolic syndrome and markers of oxidative damage

	Male (n=87)	**Female** (n=92)	**P-values**
Age (years)	42.8 (13.7)	43.9 (13.7)	0.558
Race, Chinese (%)	70 (81%)	72 (78%)	0.610
Systolic blood pressure (mmHg)	130 (15)	122 (14)	0.011
Diastolic blood pressure (mmHg)	80 (12)	78 (9)	0.374
Body mass index	24.2 (3.5)	23.1 (4.1)	0.030
High-density lipoprotein (mmol/l)	1.29 (0.38)	1.61 (0.44)	<0.001
Triglyceride (mmol/l)	1.27 (0.65)	1.05 (0.73)	0.036
Glucose (mmol/l)	5.13 (1.25)	4.75 (1.02)	0.028
Insulin (pmol/l)	8.40 (5.70-16.20)	7.10 (5.20-12.80)	0.932
HOMA-IR	1.72 (1.14-3.55)	1.47 (1.04-2.68)	0.653
Risk factor components of MetS			
None	41 (47%)	58 (63%)	0.048
1-2	39 (45%)	27 (29%)	0.010
3 and more	7 (8%)	7 (8%)	0.805

Data were expressed as absolute numbers (percentage), mean (standard deviation) or median (inter-quartile range)
Abbreviations: HOMA-IR=homeostatic model assessment-insulin resistance index, MetS=metabolic syndrome

Supplemental Table 2. Comparison between risk factors components of the metabolic syndrome in relation to markers of oxidative damage, high-sensitivity C-reactive protein and enzymatic activities in males

	Number of Risk Factor Components of the Metabolic Syndrome			P-trend
	None (n=41)	One or Two (n=39)	Metabolic syndrome (n=7)	
Age (years)	40.05 (14.03)	45.69 (13.37)	42.86 (8.57)	0.254
Race, Chinese (%)	32 (78%)	29 (74%)	5 (71%)	0.858
Insulin (pmol/l)	9.07 (6.49)	11.79 (6.97)	29.26 (28.36)	0.001
HOMA-IR	1.94 (1.42)	2.74 (1.83)	4.69 (2.00)	0.001
Blood markers				
Arachidonate (AA) (ug/ml)	95.74 (26.63)	87.25 (16.86)	81.79 (19.01)	0.080
F_2-IsoPs				
Esterified (ng/ml)	0.30 (0.09)	0.31 (0.13)	0.24 (0.97)	0.474
Free (ng/ml)	0.06 (0.02)	0.06 (0.02)	0.07 (0.02)	0.155
Esterified/AA (ng/ug)	3.33 (1.30)	3.64 (1.63)	3.02 (1.48)	0.872
HETEs				
Esterified (ng/ml)	22.42 (8.88)	23.72 (9.43)	18.60 (4.99)	0.711
Free (ng/ml)	2.18 (0.95)	2.33 (1.63)	2.48 (0.55)	0.493
Esterified/AA (ng/ug)	0.25 (0.13)	0.28 (0.11)	0.24 (0.09)	0.646
Cholesterol (mg/ml)	5.08 (0.84)	5.45 (1.06)	5.10 (0.85)	0.326
COPs (ng/ml)				
7α-OH cholesterol	20.56 (7.11)	28.41 (18.81)	25.01 (26.45)	0.069
7β-OH cholesterol	4.38 (1.65)	4.41 (1.85)	4.71 (1.61)	0.707
24-OH cholesterol	16.97 (17.52)	15.76 (10.87)	17.75 (11.36)	0.914
27-OH cholesterol	69.33 (22.00)	70.49 (28.41)	64.28 (22.92)	0.820
COPs/cholesterol (ng/mg)				
7α-OH cholesterol	4.15 (1.63)	5.50 (3.42)	5.02 (5.15)	0.113
7β-OH cholesterol	0.89 (0.43)	0.82 (0.35)	0.93 (0.32)	0.783
24-OH cholesterol	3.43 (3.32)	3.05 (2.36)	3.57 (2.37)	0.814
27-OH cholesterol	13.94 (4.70)	13.30 (5.88)	13.19 (6.44)	0.607
Uric acid, uM	353.51 (106.81)	382.97 (111.89)	364.17 (107.77)	0.420
Allantoin, uM	2.06 (0.72)	1.79 (0.69)	1.72 (0.75)	0.099
GGT (U/l)	20.90 (15.00-34.65)	29.80 (20.90-49.13)	25.90 (20.90-39.70)	0.130
Hs-CRP (mg/l)	0.72 (0.43-1.26)	1.29 (0.51-2.32) †	1.14 (0.92-5.49) †	<0.001
PAFAH activities (nmol/min/ml)	14.27 (4.48)	14.09 (4.80)	15.85 (2.11)	0.621
PLA_2 activities (mol/min/ml)	7.23 (0.96)	7.42 (2.04)	6.59 (0.93)	0.714
Urine markers				
Unadjusted (ng/ml)				
Total IsoPs	8.02 (6.08)	9.10 (5.51)	8.99 (5.67)	0.472
8-iso-F_2-IsoPs	0.79 (1.10)	0.69 (0.41)	0.75 (0.24)	0.693
2,3-dinor-F_2-IsoPs	2.81 (1.94)	2.67 (2.14)	1.85 (1.46)	0.338
2,3-dinor-5,6-dihydro-F_2-IsoPs	4.27 (4.45)	4.27 (4.45)	6.39 (5.13)	0.103
8-OHdG	2.27 (1.35)	2.64 (1.89)	3.85 (2.48)	0.093
Adjusted for creatinine (ng/mg)				
Total IsoPs	7.53 (2.77)	7.43 (3.29)	6.73 (1.75)	0.586
8-iso-F_2-IsoPs	0.51 (0.28)	0.46 (0.28)	0.30 (0.11)	0.086
2,3-dinor-F_2-IsoPs	3.34 (2.03)	3.34 (2.03)	2.07 (1.69)	0.195
2,3-dinor-5,6-dihydro-F_2-IsoPs	4.00 (2.45)	5.77 (4.41)	6.40 (5.13)	0.681
8-OHdG	0.51 (0.28)	0.46 (0.28)	0.30 (0.11)	0.086

Data were expressed as absolute numbers (percentage), mean (standard deviation) or median (inter-quartile range)
† denotes significant difference as compared with those with no risk factor (using unpaired t-test)

Abbreviations: F_2-IsoPs=F_2-isoprostanes, HETEs=hydroxyeicosatetraenoic acid, COPs=cholesterol oxidation products, 8-OHdG= 8-hydroxydeoxyguanosine, PLA_2=phospholipase A_2 activities, PAF-AH=platelet activating factor-acetylhydrolase activities, GGT=gamma glutamyltransferase, hs-CRP=high-sensitivity C-reactive protein

Supplemental Table 3. Comparison between risk factors components of the metabolic syndrome in relation to markers of oxidative damage, high-sensitivity C-reactive protein and enzymatic activities in females

	Number of Risk Factor Components of the Metabolic Syndrome			P-trend
	None (n=58)	**One or Two** (n=27)	**Metabolic syndrome** (n=7)	
Age (years)	44.29 (13.70)	42.74 (15.25)	46.29 (7.30)	0.985
Race, Chinese (%)	52 (90%)	23 (85%)	6 (86%)	0.925
Insulin (pmol/l)	7.31 (4.86)	17.51 (17.55) †	21.29 (8.81) †	<0.001
HOMA-IR	1.49 (1.13)	3.39 (3.02) †	4.89 (1.88) †	<0.001
Blood markers				
Arachidonate (AA) (ug/ml)	100.92 (26.86)	94.39 (21.61)	91.23 (19.53)	0.184
F_2-IsoPs				
Esterified (ng/ml)	0.33 (0.11)	0.32 (0.15)	0.25 (0.11)	0.128
Free (ng/ml)	0.05 (0.02)	0.05 (0.02)	0.06 (0.02)	0.939
Esterified/AA (ng/ug)	3.45 (1.21)	3.40 (1.46)	2.71 (0.99)	0.261
HETEs				
Esterified (ng/ml)	21.86 (7.14)	21.62 (7.54)	20.93 (5.81)	0.755
Free (ng/ml)	2.67 (1.44)	2.79 (1.97)	2.21 (1.05)	0.728
Esterified/AA (ng/ug)	0.23 (0.11)	0.24 (0.10)	0.24 (0.08)	0.813
Cholesterol (mg/ml)	5.41 (1.06)	5.48 (1.08)	4.91 (0.71)	0.493
COPs (ng/ml)				
7α-OH cholesterol	18.78 (6.73)	17.88 (7.84)	25.40 (12.80)	0.217
7β-OH cholesterol	4.78 (2.78)	4.34 (2.29)	4.13 (1.81)	0.382
24-OH cholesterol	14.58 (6.72)	15.01 (8.68)	17.47 (18.62)	0.475
27-OH cholesterol	58.17 (2041)	56.78 (17.54)	48.60 (10.08)	0.282
COPs/cholesterol (ng/mg)				
7α-OH cholesterol	3.59 (1.62)	3.37 (1.54)	5.12 (2.30)	0.198
7β-OH cholesterol	0.89 (0.47)	0.82 (0.45)	0.83 (0.29)	0.554
24-OH cholesterol	2.76 (1.29)	2.88 (1.94)	3.41 (3.16)	0.386
27-OH cholesterol	11.04 (4.27)	10.71 (3.99)	10.01 (2.37)	0.520
Uric acid (uM)	301.55 (138.80)	310.46 (148.44)	435.43 (244.44)	0.090
Allantoin (uM)	1.93 (0.67)	1.72 (0.65)	2.01 (0.98)	0.619
GGT (U/l)	11.35 (9.90-15.20)	13.20 (10.50-22.80)	21.20 (15.80-24.30) †	0.002
Hs-CRP (mg/l)	0.49 (0.30-1.01)	0.80 (0.56-1.41)	2.93 (2.13-10.86) †	<0.001
PAFAH activities (nmol/min/ml)	13.24 (4.33)	14.67 (3.60)	11.43 (3.20)	0.947
PLA_2 activities (mol/min/ml)	6.32 (0.97)	6.62 (0.83)	3.25 (0.36)	0.515
Urine markers				
Unadjusted (ng/ml)				
Total IsoPs	15.56 (12.34)	11.08 (7.15)	13.36 (9.62)	0.184
8-iso-F_2-IsoPs	0.57 (0.41)	0.43 (0.34)	0.47 (0.21)	0.164
2,3-dinor-F_2-IsoPs	3.58 (2.52)	2.83 (1.66)	5.15 (3.13)	0.663
2,3-dinor-5,6-dihydro-F_2-IsoPs	11.49 (11.94)	7.80 (6.30)	7.73 (1.09)	0.133
8-OHdG	2.16 (1.44)	1.96 (2.18)	2.75 (2.28)	0.981
Adjusted for creatinine (ng/mg)				
Total IsoPs	7.87 (3.11)	8.15 (2.94)	9.59 (1.54)	0.207
8-iso-F_2-IsoPs	0.59 (0.33)	0.52 (0.32)	0.44 (0.24)	0.173
2,3-dinor-F_2-IsoPs	2.28 (1.86)	2.51 (1.82)	4.07 (1.70) †	0.043
2,3-dinor-5,6-dihydro-F_2-IsoPs	5.01 (2.49)	5.11 (2.64)	5.08 (2.20)	0.875
8-OHdG	2.08 (0.98)	1.84 (0.85)	2.55 (1.04)	0.828

Data were expressed as absolute numbers (percentage), mean (standard deviation) or median (inter-quartile range)
† denotes significant difference as compared with those with no risk factor (using unpaired t-test)

Abbreviations: F_2-IsoPs=F_2-isoprostanes, HETEs=hydroxyeicosatetraenoic acid, COPs=cholesterol oxidation products, 8-OHdG= 8-hydroxydeoxyguanosine, PLA_2=phospholipase A_2 activities, PAF-AH=platelet activating factor-acetylhydrolase activities, GGT=gamma glutamyltransferase, hs-CRP=high-sensitivity C-reactive protein

Supplemental Table 4. Age-adjusted correlates of Homeostasis Model Assessment Insulin Resistance (HOMA-IR) index

	Male		Female	
	Regression coefficient	**P-values**	**Regression coefficient**	**P-values**
Plasma markers				
F_2-IsoPs				
Esterified (ng/ml)	-0.083	0.469	-0.038	0.728
Free (ng/ml)	0.121	0.292	-0.051	0.638
Esterified/AA (ng/ug)	-0.033	0.775	-0.012	0.913
HETEs				
Esterified (ng/ml)	-0.061	0.597	0.408	0.684
Free (ng/ml)	-0.083	0.472	-0.130	0.233
Esterified/AA (ng/ug)	-0.049	0.669	0.044	0.689
COPs (ng/ml)				
7α-OH cholesterol	0.336	0.004	0.238	0.290
7β-OH cholesterol	-0.052	0.653	0.339	0.001
24-OH cholesterol	0.000	0.999	0.181	0.094
27-OH cholesterol	-0.104	0.371	-0.100	0.358
COPs/cholesterol (ng/mg)				
7α-OH cholesterol	0.359	0.001	0.136	0.211
7β-OH cholesterol	-0.024	0.832	0.320	0.003
24-OH cholesterol	0.017	0.887	0.119	0.278
27-OH cholesterol	-0.081	0.479	-0.179	0.106
Uric acid (uM)	0.068	0.564	0.221	0.046
Allantoin (uM)	-0.141	0.237	-0.036	0.759
GGT (U/l)	-0.020	0.863	0.199	0.062
Hs-CRP (mg/l)	0.500	<0.001	0.285	0.007
PAFAH activities (nmol/min/ml)	-0.014	0.903	0.032	0.764
PLA_2 activities (mol/min/ml)	-0.062	0.591	0.128	0.247
Urine markers				
Unadjusted (ng/ml)				
Total F_2-IsoPs	0.049	0.674	-0.056	0.607
8-iso-F_2-IsoPs	-0.033	0.779	-0.056	0.605
2,3-dinor- F_2-IsoPs	-0.200	0.079	0.062	0.571
2,3-dinor-5,6-dihydro-F_2-IsoPs	0.174	0.132	-0.075	0.491
8-OHdG	0.150	0.264	0.147	0.239
Adjusted for creatinine (ng/mg)				
Total F_2-IsoPs	-0.130	0.273	0.141	0.205
8-iso-F_2-IsoPs	-0.130	0.265	-0.151	0.167
2,3-dinor-F_2-IsoPs	-0.335	0.004	0.102	0.351
2,3-dinor-5,6-dihydro-F_2-IsoPs	0.077	0.502	0.101	0.351
8-OHdG	-0.156	0.243	0.135	0.300

Abbreviations: F_2-IsoPs= F_2-isoprostanes, HETEs=hydroxyeicosatetraenoic acid, COPs=cholesterol oxidation products, GGT=gamma glutamyltransferase, hs-CRP=high-sensitivity C-reactive protein, PAF-AH=platelet activating factor-acetylhydrolase activities, PLA_2=phospholipase A_2 activities, 8-OHdG= 8-hydroxydeoxyguanosine