Cardiac insulin resistance in subjects with metabolic syndrome traits and early subclinical atherosclerosis

Supplementary Table 1. Characteristics by myocardial ^{18}F-FDG degree of uptake at baseline

	Total population	No uptake (grade 0)	Grade 1 uptake	Grade 2 uptake	Grade 3 uptake	p - value
n	821	156	222	222	221	
Age, years	50.6 [46.9-53.6]	50.8 [48.0-53.5]	50.7 [47.3-53.8]	50.5 [47.0-53.5]	50.0 [45.7-53.8]	0.086
Male	684 (83.7)	120 (77.4)	187 (85.0)	193 (87.3)	184 (83.3)	0.167
TBRmax	5.10 [2.75-8.04]	1.68 [1.36-2.15]	3.35 [2.58-3.91]	5.98 [5.37-6.86]	10.26 [8.81-12.27]	<0.001
Blood glucose before ^{18}FDG injection, mg/dl	89 [84-95]	92 [85-99]	90 [84-96]	88 [83-94]	89 [83-94]	<0.001
Time injection to imaging, min	132 [124-142]	134 [124-146]	130 [123-142]	131 [124-139]	132 [125-142]	0.778
Cardiovascular risk factors						
Hypertension	164 (20.1)	45 (29.0)	39 (17.7)	47 (21.3)	33 (14.9)	0.006
Dyslipidemia	479 (58.6)	86 (55.5)	134 (60.9)	139 (62.9)	120 (54.3)	0.749
Diabetes	38 (4.7)	17 (11.0)	5 (2.3)	7 (3.2)	9 (4.1)	0.016
Current smoking	217 (27.1)	45 (29.4)	61 (28.4)	65 (29.8)	46 (21.3)	0.097
Family history of CV disease	169 (20.7)	36 (23.2)	39 (17.7)	54 (24.4)	40 (18.1)	0.570
BMI, kg/m^2	27.2 ± 3.6	27.6 ± 4.1	27.3 ± 3.3	27.2 ± 3.5	26.8 ± 3.5	0.023
Body weight, kg	81.6 ± 13.7	81.3 ± 15.3	82.4 ± 13.7	82.3 ± 13.3	80.2 ± 12.8	0.352
Waist circumference, cm	93.9 ± 11.1	94.4 ± 13.3	94.4 ± 10.6	94.5 ± 10.4	92.4 ± 10.6	0.089
Metabolic syndrome and its components						
Metabolic syndrome	137 (16.8)	45 (29.0)	42 (19.1)	26 (11.8)	24 (10.9)	<0.001
Number of components						
• 0 components	261 (32.0)	44 (28.4)	67 (30.4)	69 (31.4)	81 (36.6)	0.083
• 1-2 components	418 (51.2)	66 (42.6)	111 (50.4)	125 (56..8)	116 (52.5)	0.042
• > 2 components	137 (16.8)	45 (29.0)	42 (19.1)	26 (11.8)	24 (10.9)	<0.001
Central obesity	214 (26.2)	50 (32.3)	52 (23.6)	56 (25.3)	56 (25.3)	0.265
HDL-C, mg/dL	46.4 ± 11.4	46.6 ± 12.9	46.2 ± 11.1	45.9 ± 10.3	47.0 ± 11.5	0.743
Triglycerides, mg/dL	97 [71-131]	111 [69-157]	103 [74-139]	96 [75-127]	87 [62-119]	<0.001
Fasting glucose, mg/dL	91 [85-97]	94 [87-104]	92 [85-98]	90 [85-95]	89 [83-95]	<0.001
Systolic blood pressure, mmHg	120.6 ± 12.8	120.5 ± 15.2	120.0 ± 13.0	120.3 ± 11.0	121.8 ± 12.5	0.239
Diastolic blood pressure, mmHg	75.0 ± 9.3	75.9 ± 10.6	75.0 ± 9.5	74.7 ± 8.7	74.7 ± 8.9	0.264
Treatment						
Antihypertensive therapy, n (%)	113 (13.8)	34 (21.8)	25 (11.3)	35 (15.8)	19 (8.6)	0.004
Lipid-lowering therapy, n (%)	120 (14.6)	26 (16.7)	36 (16.2)	34 (15.3)	24 (10.9)	0.094
Antidiabetic therapy, n (%)	31 (3.8)	14 (9.0)	1 (0.5)	7 (3.2)	9 (4.1)	0.163
Biochemistry						
Total cholesterol, mg/dL	208.3 ± 34.8	204.8 ± 30.1	211.0 ± 36.3	208.7 ± 36.4	207.7 ± 34.7	0.738
LDL-C, mg/dL	139.7 ± 30.9	133.4 ± 27.8	141.9 ± 32.0	140.5 ± 33.3	141.4 ± 29.0	0.049
Hemoglobin A1c, %	5.5 [5.2-5.7]	5.6 [5.3-5.8]	5.5 [5.3-5.7]	5.4 [5.2-5.7]	5.4 [5.2-5.6]	<0.001
HOMA-IR, %	1.27 [0.85-1.98]	1.64 [0.95-2.67]	1.41 [0.96-2.11]	1.24 [0.83-1.83]	1.07 [0.67-1.76]	0.002
Insulin, µU/ml	5.7 [3.9-8.3]	7.0 [4.3-10.8]	6.2 [4.4-9.1]	5.6 [3.9-7.8]	4.9 [3.3-7.5]	0.001
Inflammatory markers						
hs-CRP, mg/dL	0.11 [0.06-0.20]	0.11 [0.05-0.20]	0.11 [0.07-0.20]	0.10 [0.06-0.20]	0.10 [0.05-0.19]	0.373
Ferritin, ng/mL	122.1 [63.0-202.8]	107.7 [53.6-199.9]	137.4 [70.7-216.6]	120.5 [59.4-197.9]	121.0 [68.5-199.4]	0.227

Erythrocyte sedimentation rate (1 hour), mm	5 [4-8]	6 [4-9]	5 [4-8]	5 [4-7]	5 [4-7]	0.004
Fibrinogen, mg/dL	264.7 [236.0-295.3]	266.1 [231.8-298.1]	266.0 [237.8-297.1]	264.8 [236.5-297.6]	262.9 [236.0-291.5]	0.696
P-Selectin, ng/ml	135.2 [107.0-165.0]	136.7 [114.0-169.6]	134.8 [108.0-163.4]	135.8 [109.7-165.2]	131.7 [103.5-170.3]	0.631
Vascular cell adhesion molecule-1, ng/ml	644.8 [519.6-820.0]	640.8 [512.7-814.5]	656.4 [516.9-816.6]	619.6 [505.8-837.8]	661.4 [544.8-813.0]	0.648
Blood count						
Red blood cell count, 10^6 cells/µL	5.86 [5.01-7.02]	6.22 [5.28-7.38]	5.81 [4.95-7.02]	5.77 [4.96-6.90]	5.83 [4.97-6.88]	0.016
Hemoglobin, g/dL	15.0 [14.3-15.6]	14.8 [14.1-15.6]	15.0 [14.3-15.7]	15.0 [14.3-15.6]	15.1 [14.3-15.7]	0.095
Platelet count, 10^3 cells/µL	225 [199-256]	227 [197-263]	227 [198-254]	220 [199-252]	229 [199-259]	0.565
Leucocytes, 10^3 cells/µL	5.86 [5.01-7.02]	6.22 [5.28-7.38]	5.81 [4.95-7.02]	5.77 [4.96-6.90]	5.83 [4.97-6.88]	0.016
Segmented neutrophils, 10^3 cells/µL	3.33 [2.72-4.21]	3.50 [2.83-4.51]	3.32 [2.72-4.19]	3.28 [2.74-4.10]	3.26 [2.60-4.06]	0.021
Lymphocytes, 10^3 cells/µL	1.85 [1.56-2.20]	1.97 [1.66-2.34]	1.89 [1.56-2.23]	1.83 [1.53-2.12]	1.81 [1.58-2.12]	0.172
Monocytes, 10^3 cells/µL	0.42 [0.33-0.52]	0.42 [0.34-0.53]	0.42 [0.34-0.53]	0.42 [0.33-0.53]	0.41 [0.33-0.48]	0.105
Eosinophils, 10^3 cells/µL	0.13 [0.08-0.20]	0.13 [0.09-0.21]	0.13 [0.08-0.19]	0.13 [0.08-0.21]	0.12 [0.08-0.18]	0.719
Basophils, 10^3 cells/µL	0.05 [0.03-0.06]	0.05 [0.03-0.07]	0.05 [0.03-0.06]	0.05 [0.03-0.06]	0.05 [0.03-0.06]	0.512

Data are presented as n (%) or median [Q1-Q3].
*hs-CRP= high-sensitivity C-reactive protein.

Supplementary Table 2: Characteristics by quantitative measurements of myocardial ^{18}F-FDG degree of uptake at baseline

| | Total population | TBRmax Quartile | | | | p-value |
		Quartile 1	Quartile 2	Quartile 3	Quartile 4	
n	821	206	205	205	205	
Age, years	50.6 [46.9-53.6]	51.1 [48.0-53.7]	50.7 [47.3-53.9]	50.3 [46.7-53.2]	50.0 [45.6-53.8]	0.039
Male	684 (83.7)	162 (79.0)	175 (86.2)	178 (87.3)	169 (82.4)	0.327
TBRmax	5.10 [2.75-8.04]	1.81 [1.44-2.31]	3.82 [3.28-4.46]	6.32 [5.71-7.13]	10.56 [9.09-12.65]	<0.001
Blood glucose before ^{18}FDG injection, mg/dl	89 [84-95]	90 [85-98]	90 [84-97]	88 [83-94]	89 [83-94]	<0.001
Time injection to imaging, min	132 [124-142]	134 [125-145]	131 [123-142]	131 [124-139]	133 [124-142]	0.442
Cardiovascular risk factors						
Hypertension	164 (20.1)	54 (26.3)	39 (19.2)	38 (18.6)	33 (16.1)	0.012
Dyslipidemia	479 (58.6)	114 (55.6)	127 (62.6)	130 (63.7)	108 (52.7)	0.621
Diabetes	38 (4.7)	20 (9.8)	5 (2.5)	5 (2.5)	8 (3.9)	0.008
Current smoking	217 (27.1)	61 (29.9)	49 (25.0)	62 (30.7)	45 (22.5)	0.237
Family history of CV disease	169 (20.7)	46 (22.4)	37 (18.2)	48 (23.5)	38 (18.5)	0.611
BMI, kg/m^2	27.2 ± 3.6	27.5 ± 3.9	27.5 ± 3.5	27.1 ± 3.4	26.8 ± 3.6	0.031
Body weight, kg	81.6 ± 13.7	81.7 ± 14.9	82.3 ± 13.4	82.1 ± 13.6	80.2 ± 12.8	0.262
Waist circumference, cm	93.9 ± 11.1	94.7 ± 12.6	94.2 ± 10.5	94.2 ± 10.5	92.5 ± 10.6	0.059
Metabolic syndrome and its components						
Metabolic syndrome	137 (16.8)	56 (27.3)	34 (16.7)	23 (11.3)	24 (11.7)	<0.001
Number of components						
• 0 components	261 (32.0)	61 (29.8)	62 (30.5)	62 (30.6)	76 (37.1)	0.252
• 1-2 components	418 (51.2)	88 (42.9)	107 (52.7)	118 (58.1)	105 (51.2)	0.068
• >2 components	137 (16.8)	56 (27.3)	34 (16.8)	23 (11.3)	24 (11.7)	<0.001
Central obesity	214 (26.2)	61 (29.8)	51 (25.1)	49 (24.0)	53 (25.9)	0.351
HDL-C, mg/dL	46.4 ± 11.4	46.3 ± 12.2	46.6 ± 11.2	45.5 ± 10.4	47.0 ± 11.7	0.773
Triglycerides, mg/dL	97 [71-131]	110 [72-150]	98 [72-133]	99 [75-130]	87 [62-118]	<0.001
Fasting glucose, mg/dL	91 [85-97]	93 [85-101]	91 [85-98]	90 [85-96]	89 [83-95]	<0.001
Systolic blood pressure, mmHg	120.6 ± 12.8	119.8 ± 13.9	121.0 ± 13.7	119.7 ± 10.7	122.1 ± 12.7	0.147
Diastolic blood pressure, mmHg	75.0 ± 9.3	75.4 ± 10.3	75.6 ± 9.5	74.2 ± 8.4	74.9 ± 9.2	0.335
Treatment						
Antihypertensive therapy	113 (13.8)	41 (19.9)	25 (12.2)	29 (14.1)	18 (8.8)	0.003
Lipid-lowering therapy	120 (14.6)	32 (15.5)	37 (18.0)	27 (13.2)	24 (11.7)	0.139
Antidiabetic therapy	31 (3.8)	14 (6.8)	4 (2.0)	5 (2.4)	8 (3.9)	0.167
Biochemistry						
Total cholesterol, mg/dL	208.3 ± 34.8	204.0 ± 30.5	213.0 ± 36.6	209.3 ± 36.7	207.0 ± 34.7	0.635
LDL-C, mg/dL	139.7 ± 30.9	133.3 ± 27.9	143.9 ± 32.0	141.1 ± 33.7	140.7 ± 28.8	0.046
Hemoglobin A1c, %	5.5 [5.2-5.7]	5.5 [5.3-5.8]	5.5 [5.3-5.7]	5.4 [5.2-5.7]	5.4 [5.2-5.6]	0.001
HOMA-IR, %	1.27 [0.85-1.98]	1.53 [0.95-2.51]	1.33 [0.92-2.11]	1.24 [0.83-1.87]	1.09 [0.68-1.75]	0.006
Insulin, µU/ml	5.7 [3.9-8.3]	6.6 [4.3-9.8]	6.0 [4.3-9.2]	5.6 [3.9-8.0]	4.9 [3.4-7.5]	0.002
Inflammatory markers						
hs-CRP, mg/dL	0.11 [0.06-0.20]	0.11 [0.06-0.20]	0.11 [0.06-0.20]	0.11 [0.06-0.21]	0.09 [0.05-0.18]	0.418
Ferritin, ng/mL	122.1 [63.0-202.8]	122.8 [56.7-207.3]	131.9 [75.2-208.4]	114.1 [57.5-197.9]	124.1 [66.9-200.5]	0.326
Erythrocyte sedimentation rate (1 hour), mm	5 [4-8]	6 [4-8]	5 [4-8]	5 [4-7]	5 [4-7]	0.010
Fibrinogen, mg/dL	264.7 [236.0-295.3]	270.0 [233.7-302.8]	260.6 [235.8-291.8]	268.8 [239.4-298.4]	261.9 [236.0-291.5]	0.472
P-Selectin, ng/ml	135.2 [107.0-165.0]	137.7 [111.5-164.5]	134.6 [109.9-164.1]	134.4 [103.4-166.7]	133.5 [105.3-170.1]	0.546
Vascular cell adhesion molecule-1, ng/ml	644.8 [519.6-820.0]	636.1 [504.3-810.0]	665.2 [518.6-818.6]	623.6 [518.3-824.2]	658.4 [543.5-828.5]	0.485

Blood count						
Red blood cell count, 10^6 cells/µL	5.86 [5.01-7.02]	6.11 [5.18-7.27]	5.92 [4.94-6.91]	5.75 [4.97-6.89]	5.83 [4.99-6.88]	0.032
Hemoglobin, g/dL	15.0 [14.3-15.6]	15.0 [14.3-15.7]	14.9 [14.2-15.6]	15.1 [14.3-15.6]	15.0 [14.3-15.6]	0.363
Platelet count, 10^3 cells/µL	225 [199-256]	224 [196-256]	227 [197-254]	222 [203-255]	228 [198-259]	0.909
Leucocytes, 10^3 cells/µL	5.86 [5.01-7.02]	6.11 [5.18-7.27]	5.92 [4.94-6.91]	5.75 [4.97-6.89]	5.83 [4.99-6.88]	0.032
Segmented neutrophils, 10^3 cells/µL	3.33 [2.72-4.21]	3.49 [2.78-4.41]	3.35 [2.72-4.13]	3.23 [2.73-4.10]	3.27 [2.60-4.06]	0.043
Lymphocytes, 10^3 cells/µL	1.85 [1.56-2.20]	1.95 [1.62-2.27]	1.87 [1.56-2.26]	1.82 [1.52-2.12]	1.81 [1.56-2.11]	0.243
Monocytes, 10^3 cells/µL	0.42 [0.33-0.52]	0.42 [0.35-0.54]	0.42 [0.33-0.53]	0.42 [0.33-0.52]	0.40 [0.33-0.48]	0.082
Eosinophils, 10^3 cells/µL	0.13 [0.08-0.20]	0.13 [0.09-0.20]	0.13 [0.08-0.20]	0.13 [0.09-0.22]	0.12 [0.08-0.18]	0.714
Basophils, 10^3 cells/µL	0.05 [0.03-0.06]	0.05 [0.03-0.07]	0.05 [0.03-0.07]	0.04 [0.03-0.06]	0.05 [0.03-0.06]	0.286

Data are presented as n (%) or median [Q1-Q3].
*hs-CRP= high-sensitivity C-reactive protein.

Supplementary Table 3. Multivariable analyses: Associations between metabolic syndrome and myocardial ^{18}F-FDG uptake (TBRmax).

	Myocardial uptake (TBRmax) at baseline			Myocardial uptake (TBRmax) at follow-up		
	Unadjusted	**Model 1††**	**Model 2††**	**Unadjusted**	**Model 1††**	**Model 2††**
Metabolic Syndrome at baseline†	-1.40 (-2.13; -0.68) p<0.001	-1.33 (-2.07; -0.58) p=0.001	-1.43 (-2.16; -0.69) p<0.001	-1.3 (-2.38; -0.26) p=0.015	-1.10 (-2.20; -0.002) p=0.050	-1.38 (-2.46; -0.30) p=0.012
HOMA-IR at baseline†	-0.15 (-0.25; 0.05) p=0.003	-0.11 (-0.22; 0.004) p=0.059	-0.15 (-0.25; 0.05) p=0.003	-0.70 (-1.02; -0.37) p<0.001	-0.58 (-0.93; -0.24) p=0.001	-0.74 (-1.08; 0.41) p<0.001
Metabolic Syndrome at follow-up†	n/a	n/a	n/a	-1.56 (-2.55; -0.57) p=0.002	-1.45 (-2.48; 0.42) p=0.006	-1.58 (-2.58; 0.58) p=0.002
HOMA-IR at follow-up†	n/a	n/a	n/a	-0.56 (-0.84; -0.28) p<0.001	-0.53 (-0.82;-0.24) p<0.001	-0.60 (-0.88; 0.32) p<0.001

†Beta-coefficients, confidence intervals, and p-values obtained from a linear regression to evaluate the effect of metabolic syndrome on TBRmax.
††Model 1: adjusted by blood glucose before injection and time from injection to imaging acquisition; Model 2: adjusted by age and sex.

Supplementary Table 4. Vascular and bone marrow ^{18}F-FDG uptake by presence of myocardial ^{18}F-FDG uptake

	Total population	No uptake (grade 0)	Uptake (grade 1-3)	p-value
Arterial ^{18}F-FDG uptake (n=818)				
Presence of uptake	391 (47.8)	30 (58.1)	301 (45.4)	0.004
Number of uptakes	0 [0-2]	1 [0-2]	0 [0-1]	0.003
SUVmax arterial uptake	1.38 ± 0.19	1.43 ± 0.18	1.37 ± 0.20	0.019
Bone marrow ^{18}F-FDG uptake (n=736)				
Bone marrow SUVmax	1.90 ± 0.42	1.97 ± 0.43	1.88 ± 0.42	0.051
Bone marrow activation†	367 (49.9)	82 (60.3)	258 (47.5)	0.007

Data are presented as median [Q1-Q3].
† BM activation was defined when mean BM SUVmax was above the median value (SUVmax 1.9).

Supplementary Table 5: Associations between vascular, bone marrow and myocardial ^{18}F-FDG uptake, by grade of myocardial ^{18}F-FDG uptake

	Total population	No uptake (grade 0)	Grade 1 Uptake	Grade 2 Uptake	Grade 3 Uptake	p trend
Arterial ^{18}F-FDG uptake (n=818)						
Presence of uptake	391 (47.8)	90 (58.1)	109 (49.1)	106 (48.0)	86 (39.1)	<0.001
Number of uptakes	0 [0-2]	1 [0-2]	0 [0-2]	0 [0-1]	0 [0-1]	0.001
SUVmax arterial uptake	1.38 ± 0.19	1.43 ± 0.18	1.40 ± 0.19	1.37 ± 0.19	1.31 ± 0.20	<0.001
Bone marrow ^{18}F-FDG uptake (n=736)						
Bone marrow SUVmax	1.9 ± 0.42	1.97 ± 0.43	1.96 ± 0.43	1.84 ± 0.41	1.84 ± 0.42	0.002
Bone marrow activation †	367 (49.9)	82 (60.3)	113 (55.1)	84 (42.2)	88 (44.9)	<0.001

Data are presented as median [Q1-Q3].

† BM activation was defined when mean BM SUVmax was above the median value (SUVmax 1.9).

Supplementary Table 6. Characteristics by presence of myocardial ^{18}F-FDG uptake at follow-up

	Total population	No uptake (grade 0)	Uptake (grade 1-3)	p-value
n	**700**	**70**	**630**	
Age, years	55.2 [51.7-58.2]	55.1 [53.2-57.6]	55.2 [51.6-58.4]	0.964
Male	584 (83.4)	60 (85.7)	524 (83.2)	0.588
TBRmax	5.60 [3.28-9.88]	1.75 [1.49-2.00]	6.18 [3.79-10.44]	<0.001
Blood glucose before injection, mg/dl	95 [87-103]	100 [87-117]	94 [87-103]	0.027
Time injection to imaging, min	128 [118-139]	127 [117-139]	128 [118-139]	0.752
Cardiovascular risk factors				
Hypertension	197 (29.2)	24 (36.4)	173 (28.5)	0.180
Dyslipidemia	394 (56.3)	39 (55.7)	355 (56.3)	0.919
Diabetes	39 (5.6)	15 (21.4)	24 (3.8)	<0.001
Current smoking	136 (20.1)	12 (18.2)	124 (20.3)	0.680
Family history of CV disease	110 (16.3)	10 (15.2)	100 (16.5)	0.783
BMI, kg/m^2	27.2 ± 3.7	28.5 ± 3.9	27.1 ± 3.7	0.004
Body weight, kg	81.9 ± 13.7	84.7 ± 13.4	81.6 ± 13.7	0.079
Waist circumference, cm	95.9 ± 11.4	98.9 ± 12.5	95.6 ± 11.2	0.024
Metabolic syndrome and its components				
Metabolic syndrome	107 (15.9)	16 (24.2)	91 (15.0)	0.051
Number of components				
• 0 components	254 (37.7)	16 (24.2)	238 (39.2)	0.017
• 1-2 components	312 (46.4)	34 (51.5)	278 (45.8)	0.376
• >2 components	107 (15.9)	16 (24.2)	91 (15.0)	0.051
Central obesity	262 (37.4)	32 (45.7)	230 (36.5)	0.131
HDL-C, mg/dL	51.0 ± 13.2	47.8 ± 13.0	51.4 ± 13.1	0.032
Triglycerides, mg/dL	93 [69-131]	126 [82-161]	91 [67-126]	0.001
Fasting glucose, mg/dL	89 [83-96]	96 [89-106]	88 [83-96]	<0.001
Systolic blood pressure, mmHg	121.0 ± 13.5	119.9 ± 12.6	121.2 ± 13.6	0.462
Diastolic blood pressure, mmHg	74.7 ± 8.7	74.1 ± 8.5	74.7 ± 8.7	0.582
Treatment				
Antihypertensive therapy	156 (22.3)	22 (31.4)	134 (21.3)	0.053
Lipid-lowering therapy	180 (25.7)	19 (27.1)	161 (25.6)	0.773
Antidiabetic therapy	35 (5.0)	14 (20.0)	21 (3.3)	<0.001
Biochemistry				
Total cholesterol, mg/dL	205.6 ± 38.9	198.7 ± 41.0	206.4 ± 38.6	0.119
LDL-C, mg/dL	133.0 ± 34.0	125.5 ± 38.4	133.8 ± 33.4	0.051
Hemoglobin A1c, %	5.4 [5.2-5.7]	5.6 [5.4-6.2]	5.4 [5.2-5.7]	<0.001
HOMA-IR, %	1.39 [0.95-2.17]	2.05 [1.28-3.43]	1.35 [0.93-2.02]	<0.001
Insulin, µU/ml	6.4 [4.5-9.4]	8.5 [5.6-13.4]	6.3 [4.3-9.1]	<0.001
Inflammatory markers				
hs-CRP, mg/dL	0.14 [0.07-0.38]	0.14 [0.06-0.36]	0.14 [0.07-0.38]	0.808
Ferritin, ng/mL	128.5 [69.9-213.1]	132.2 [74.7-235.6]	127.9 [69.8-206.3]	0.262
Erythrocyte sedimentation rate (1 hour), mm	6 [5-9]	7 [5-9]	6 [5-9]	0.440
Fibrinogen, mg/dL	243.5 [212.6-283.5]	237.0 [208.0-288.4]	243.5 [214.0-283.3]	0.631
P-selectin, ng/ml	113.6 [87.7-154.0]	124.5 [97.3-157.3]	112.2 [86.0-153.1]	0.108
Vascular cell adhesion molecule-1, ng/ml	619.9 [466.6-796.4]	543.6 [459.4-826.3]	627.6 [471.3-794.3]	0.403
Blood count				
Red blood cell count, 10^6 cells/µL	5.89 [4.94-6.90]	6.27 [5.38-7.03]	5.86 [4.90-6.85]	0.069
Hemoglobin, g/dL	15.3 [14.5-16.0]	15.6 [14.6-16.1]	15.3 [14.5-16.0]	0.192
Platelet count, 10^3 cells/µL	217 [189-251]	214 [189-241]	218 [189-252]	0.509
Leucocytes, 10^3 cells/µL	5.89 [4.94-6.90]	6.27 [5.38-7.03]	5.86 [4.90-6.85]	0.069
Segmented neutrophils, 10^3 cells/µL	3.36 [2.73-4.10]	3.50 [2.80-4.19]	3.34 [2.72-4.09]	0.294
Lymphocytes, 10^3 cells/µL	1.80 [1.49-2.23]	1.88 [1.62-2.39]	1.78 [1.48-2.21]	0.061
Monocytes, 10^3 cells/µL	0.41 [0.32-0.53]	0.42 [0.32-0.55]	0.41 [0.32-0.52]	0.969
Eosinophils, 10^3 cells/µL	0.13 [0.09-0.20]	0.16 [0.11-0.23]	0.13 [0.09-0.20]	0.050
Basophils, 10^3 cells/µL	0.05 [0.03-0.07]	0.05 [0.03-0.07]	0.05 [0.03-0.07]	0.339

Data are presented as n (%) or median [Q1-Q3].*hs-CRP= high-sensitivity C-reactive protein.

Supplementary Table 7. Characteristics by myocardial ^{18}F-FDG degree of uptake at follow-up

	Total population	No uptake (Grade 0)	Uptake (Grade 1)	Uptake (Grade 2)	Uptake (Grade 3)	p-value
n	700	70	210	210	210	
Age, years	55.2 [51.7-58.2]	55.1 [53.2-57.6]	55.5 [51.5-58.6]	55.7 [52.2-58.5]	54.2 [51.0-58.1]	0.277
Men	584 (83.4)	60 (85.7)	168 (80.0)	178 (84.8)	178 (84.8)	0.481
TBRmax	5.60 [3.28-9.88]	1.75 [1.49-2.00]	3.26 [2.64-3.79]	6.18 [5.34-7.42]	11.76 [10.44-15.06]	<0.001
Blood glucose before ^{18}FDG injection, mg/dl	95 [87-103]	100 [87-117]	92 [85-103]	95 [87-103]	95 [88-103]	0.009
Time injection to imaging, min	128 [118-139]	127 [117-139]	129 [118-140]	127 [117-137]	130 [119-141]	0.414
Cardiovascular risk factors						
Hypertension	197 (29.2)	24 (36.4)	55 (27.8)	67 (33.0)	51 (24.6)	0.166
Dyslipidemia	394 (56.3)	39 (55.7)	122 (58.1)	123 (58.6)	110 (52.4)	0.384
Diabetes	39 (5.6)	15 (21.4)	11 (5.2)	8 (3.8)	5 (2.4)	<0.001
Current smoking	136 (20.1)	12 (18.2)	43 (21.6)	47 (23.0)	34 (16.4)	0.430
Family history of CV disease	110 (16.3)	10 (15.2)	27 (13.7)	42 (20.7)	31 (15.0)	0.675
BMI, kg/m^2	27.2 ± 3.7	28.5 ± 3.9	27.4 ± 3.9	26.9 ± 3.7	26.9 ± 3.4	0.006
Body weight, kg	81.9 ± 13.7	84.7 ± 13.4	81.9 ± 14.3	80.8 ± 13.3	82.1 ± 13.7	0.364
Waist circumference, cm	95.9 ± 11.4	98.9 ± 12.5	96.6 ± 12.1	95.5 ± 10.7	94.8 ± 10.9	0.008
Metabolic syndrome and its components						
Metabolic syndrome	107 (15.9)	16 (24.2)	41 (20.8)	28 (13.8)	22 (10.6)	0.001
Number of components						
• 0 components	254 (37.7)	16 (24.2)	67 (34.0)	84 (41.4)	87 (42.0)	0.006
• 1-2 components	312 (46.4)	34 (51.5)	89 (45.2)	91 (44.8)	98 (47.3)	0.847
• > 2 components	107 (15.9)	16 (24.2)	41 (20.8)	28 (13.8)	22 (10.6)	0.001
Central obesity	262 (37.4)	32 (45.7)	99 (47.1)	71 (33.8)	60 (28.6)	<0.001
HDL-C, mg/dL	51.0 ± 13.2	47.8 ± 13.0	51.3 ± 14.8	51.5 ± 12.3	51.3 ± 12.2	0.191
Triglycerides, mg/dL	93 [69-131]	126 [82-161]	101 [73-142]	96 [71-125]	81 [61-110]	<0.001
Fasting glucose, mg/dL	89 [83-96]	96 [89-106]	89 [82-96]	88 [83-95]	87 [82-94]	<0.001
Systolic blood pressure, mmHg	121.0 ± 13.5	119.9 ± 12.6	119.8 ± 13.3	122.4 ± 14.3	121.3 ± 13.1	0.205
Diastolic blood pressure, mmHg	74.7 ± 8.7	74.1 ± 8.5	74.6 ± 8.2	75.0 ± 9.0	74.6 ± 8.9	0.713
Treatment						
Antihypertensive therapy, n (%)	156 (22.3)	22 (31.4)	46 (21.9)	52 (24.8)	36 (17.1)	0.035
Lipid-lowering therapy, n (%)	180 (25.7)	19 (27.1)	60 (28.6)	56 (26.7)	45 (21.4)	0.134
Antidiabetic therapy, n (%)	35 (5.0)	14 (20.0)	10 (4.8)	8 (3.8)	3 (1.4)	<0.001
Biochemistry						
Total cholesterol, mg/dL	205.6 ± 38.9	198.7 ± 41.0	206.1 ± 38.4	209.7 ± 39.7	203.4 ± 37.6	0.693
LDL-C, mg/dL	133.0 ± 34.0	125.5 ± 38.4	131.6 ± 32.2	137.1 ± 34.7	132.8 ± 33.1	0.143
Hemoglobin A1c, %	5.4 [5.2-5.7]	5.6 [5.4-6.2]	5.4 [5.2-5.7]	5.5 [5.2-5.7]	5.4 [5.2-5.7]	<0.001
HOMA-IR, %	1.39 [0.95-2.17]	2.05 [1.28-3.43]	1.45 [0.95-2.34]	1.38 [0.96-2.02]	1.20 [0.87-1.75]	<0.001
Insulin, µU/ml	6.4 [4.5-9.4]	8.5 [5.6-13.4]	6.5 [4.7-9.7]	6.3 [4.4-9.1]	5.6 [4.0-8.2]	<0.001
Inflammatory markers						
hs-CRP, mg/dL	0.14 [0.07-0.38]	0.14 [0.06-0.36]	0.17 [0.08-0.44]	0.13 [0.06-0.50]	0.12 [0.06-0.27]	0.111
Ferritin, ng/mL	128.5 [69.9-213.1]	132.2 [74.7-235.6]	136.8 [69.3-238.9]	121.7 [75.2-192.2]	120.9 [68.9-196.9]	0.005
Erythrocyte sedimentation rate (1 hour), mm	6 [5-9]	7 [5-9]	7 [5-11]	6 [4-9]	6 [5-9]	0.303
Fibrinogen, mg/dL	243.5 [212.6-283.5]	237.0 [208.0-288.4]	246.3 [212.6-285.6]	242.0 [218.9-289.8]	243.5 [211.0-275.7]	0.606
P-Selectin, ng/ml	113.6 [87.7-154.0]	124.5 [97.3-157.3]	113.0 [84.2-156.6]	115.1 [89.0-149.9]	107.9 [84.8-152.0]	0.120
Vascular cell adhesion molecule-1, ng/ml	619.9 [466.6-796.4]	543.6 [459.4-826.3]	613.5 [455.5-786.3]	626.2 [468.8-792.8]	641.7 [483.6-810.8]	0.290
Blood count						
Red blood cell count, 10^6 cells/µL	5.89 [4.94-6.90]	6.27 [5.38-7.03]	6.26 [4.99-7.08]	5.85 [4.90-7.01]	5.62 [4.86-6.55]	0.007
Hemoglobin, g/dL	15.3 [14.5-16.0]	15.6 [14.6-16.1]	15.3 [14.4-16.1]	15.3 [14.5-16.0]	15.2 [14.5-15.9]	0.301

Platelet count, 10^3 cells/µL	217 [189-251]	214 [189-241]	214 [185-251]	222 [190-255]	218 [188-249]	0.412
Leucocytes, 10^3 cells/µL	5.89 [4.94-6.90]	6.27 [5.38-7.03]	6.26 [4.99-7.08]	5.85 [4.90-7.01]	5.62 [4.86-6.55]	0.007
Segmented neutrophils, 10^3 cells/µL	3.36 [2.73-4.10]	3.50 [2.80-4.19]	3.45 [2.91-4.10]	3.35 [2.68-4.33]	3.23 [2.59-3.81]	0.021
Lymphocytes, 10^3 cells/µL	1.80 [1.49-2.23]	1.88 [1.62-2.39]	1.93 [1.51-2.31]	1.77 [1.49-2.13]	1.73 [1.46-2.16]	0.011
Monocytes, 10^3 cells/µL	0.41 [0.32-0.53]	0.42 [0.32-0.55]	0.42 [0.32-0.53]	0.40 [0.33-0.53]	0.41 [0.32-0.52]	0.869
Eosinophils, 10^3 cells/µL	0.13 [0.09-0.20]	0.16 [0.11-0.23]	0.13 [0.09-0.20]	0.14 [0.08-0.23]	0.12 [0.09-0.19]	0.269
Basophils, 10^3 cells/µL	0.05 [0.03-0.07]	0.05 [0.03-0.07]	0.05 [0.03-0.07]	0.05 [0.03-0.07]	0.05 [0.04-0.07]	0.908

Data are presented as n (%) or median [Q1-Q3].
*hs-CRP= high-sensitivity C-reactive protein.

Supplementary Table 8: Myocardial ^{18}F-FDG uptake according to number of components of the Metabolic Syndrome

	Metabolic syndrome components				p-trend
	0	1-2	>2		
n	254	312	107		
TBRmax	6.29 [3.58-10.61]	5.58 [3.32-9.97]	4.22 [2.67-8.10]		0.005

Supplementary Table 9: Characteristics by quantitative measurements of myocardial ^{18}F-FDG degree of uptake at follow-up

		TBRmax Quartile				
	Total population	**Quartile 1**	**Quartile 2**	**Quartile 3**	**Quartile 4**	**p-value**
n	700	175	175	175	175	
Age, years	55.2 [51.7-58.2]	55.2 [51.7-58.1]	55.6 [52.0-58.4]	56.1 [52.4-58.8]	54.0 [50.6-58.0]	0.243
Male	584 (83.4)	142 (81.1)	143 (81.7)	149 (85.1)	150 (85.7)	0.173
TBRmax	5.60 [3.28-9.88]	2.19 [1.75-2.70]	4.33 [3.69-4.99]	7.42 [6.45-8.52]	12.43 [11.12-15.80]	<0.001
Blood glucose before ^{18}FDG injection, mg/dl	95 [87-103]	94 [87-105]	93 [87-103]	95 [87-103]	95 [88-103]	0.058
Time injection to imaging, min	128 [118-139]	129 [117-139]	128 [118-140]	127 [118-137]	130 [119-140]	0.292
Cardiovascular risk factors						
Hypertension	197 (29.2)	52 (31.7)	49 (29.2)	56 (32.9)	40 (23.3)	0.165
Dyslipidemia	394 (56.3)	100 (57.1)	103 (58.9)	104 (59.4)	87 (49.7)	0.196
Diabetes	39 (5.6)	19 (10.9)	10 (5.7)	6 (3.4)	4 (2.3)	<0.001
Current smoking	136 (20.1)	36 (22.0)	36 (21.3)	37 (21.6)	27 (15.7)	0.179
Family history of CV disease	110 (16.3)	23 (14.1)	28 (16.7)	32 (18.8)	27 (15.7)	0.599
BMI, kg/m^2	27.2 ± 3.7	27.7 ± 3.8	27.3 ± 4.1	27.1 ± 3.7	26.7 ± 3.4	0.012
Body weight, kg	81.9 ± 13.7	82.8 ± 14.0	81.5 ± 14.4	81.6 ± 13.0	81.8 ± 13.6	0.534
Waist circumference, cm	95.9 ± 11.4	97.5 ± 12.1	96.2 ± 11.7	95.7 ± 10.8	94.3 ± 10.7	0.010
Metabolic syndrome and its components						
Metabolic syndrome	107 (15.9)	38 (23.3)	28 (16.7)	25 (14.7)	16 (9.3)	0.001
Number of components						
• 0 components	254 (37.7)	51 (31.3)	57 (33.9)	69 (40.6)	77 (44.8)	0.005
• 1-2 components	312 (46.4)	74 (45.4)	83 (49.4)	76 (44.7)	79 (45.9)	0.851
• >2 components	107 (15.9)	38 (23.3)	28 (16.7)	25 (14.7)	16 (9.3)	0.001
Central obesity	262 (37.4)	84 (48.0)	73 (41.7)	58 (33.1)	47 (26.9)	<0.001
HDL-C, mg/dL	51.0 ± 13.2	49.8 ± 14.8	51.1 ± 13.3	51.1 ± 12.3	52.0 ± 12.1	0.136
Triglycerides, mg/dL	93 [69-131]	113 [77-150]	94 [72-144]	97 [70-124]	80 [60-107]	<0.001
Fasting glucose, mg/dL	89 [83-96]	92 [85-101]	89 [81-95]	88 [83-95]	88 [82-95]	<0.001
Systolic blood pressure, mmHg	121.0 ± 13.5	119.0 ± 12.5	121.8 ± 14.2	121.4 ± 13.7	122.0 ± 13.4	0.077
Diastolic blood pressure, mmHg	74.7 ± 8.7	73.7 ± 8.2	75.6 ± 8.9	74.4 ± 8.6	74.9 ± 9.0	0.461
Treatment						
Antihypertensive therapy	156 (22.3)	47 (26.9)	36 (20.6)	48 (27.4)	25 (14.3)	0.028
Lipid-lowering therapy	180 (25.7)	48 (27.4)	52 (29.7)	46 (26.3)	34 (19.4)	0.064
Antidiabetic therapy	35 (5.0)	18 (10.3)	9 (5.1)	6 (3.4)	2 (1.1)	<0.001
Biochemistry						
Total cholesterol, mg/dL	205.6 ± 38.9	203.4 ± 42.9	206.1 ± 34.0	206.6 ± 40.6	206.4 ± 37.7	0.467
LDL-C, mg/dL	133.0 ± 34.0	129.4 ± 36.8	132.8 ± 30.1	134.8 ± 35.4	135.1 ± 33.2	0.096
Hemoglobin A1c, %	5.4 [5.2-5.7]	5.5 [5.3-5.8]	5.4 [5.2-5.7]	5.5 [5.3-5.7]	5.4 [5.2-5.7]	<0.001
HOMA-IR, %	1.39 [0.95-2.17]	1.59 [1.02-2.75]	1.45 [1.03-2.22]	1.38 [0.95-2.00]	1.19 [0.85-1.74]	<0.001
Insulin, µU/ml	6.4 [4.5-9.4]	6.7 [4.8-11.2]	6.5 [4.9-9.4]	6.1 [4.2-9.1]	5.4 [4.0-8.1]	<0.001
Inflammatory markers						
hs-CRP, mg/dL	0.14 [0.07-0.38]	0.16 [0.08-0.37]	0.14 [0.07-0.48]	0.13 [0.06-0.57]	0.12 [0.06-0.27]	0.191
Ferritin, ng/mL	128.5 [69.9-213.1]	133.0 [74.4-224.1]	134.8 [69.3-239.0]	117.5 [69.8-192.2]	128.2 [69.0-198.8]	0.005
Erythrocyte sedimentation rate (1 hour), mm	6 [5-9]	7 [5-11]	6 [4-9]	6 [4-8]	6 [5-9]	0.305
Fibrinogen, mg/dL	243.5 [212.6-283.5]	243.5 [212.6-287.0]	247.3 [209.1-282.1]	240.6 [220.3-288.4]	244.9 [211.2-277.8]	0.771
P-Selectin, ng/ml	113.6 [87.7-154.0]	121.0 [88.5-157.3]	114.1 [89.7-154.0]	113.8 [88.0-148.3]	108.1 [84.8-158.3]	0.226
Vascular cell adhesion molecule-1, ng/ml	619.9 [466.6-796.4]	578.8 [451.1-791.6]	628.2 [481.8-800.5]	604.3 [480.8-774.0]	646.3 [479.1-818.4]	0.370
Blood count						
Red blood cell count, 10^6 cells/µL	5.89 [4.94-6.90]	6.32 [5.10-7.03]	5.99 [4.97-7.08]	5.90 [4.90-6.91]	5.50 [4.80-6.44]	0.003
Hemoglobin, g/dL	15.3 [14.5-16.0]	15.3 [14.5-16.1]	15.4 [14.5-16.0]	15.2 [14.5-15.9]	15.2 [14.5-15.9]	0.643

Platelet count, 10^3 cells/µL	217 [189-251]	217 [189-251]	211 [185-249]	222 [189-254]	218 [191-251]	0.385
Leucocytes, 10^3 cells/µL	5.89 [4.94-6.90]	6.32 [5.10-7.03]	5.99 [4.97-7.08]	5.90 [4.90-6.91]	5.50 [4.80-6.44]	0.003
Segmented neutrophils, 10^3 cells/µL	3.36 [2.73-4.10]	3.49 [2.86-4.12]	3.41 [2.86-4.27]	3.34 [2.69-4.14]	3.18 [2.56-3.79]	0.010
Lymphocytes, 10^3 cells/µL	1.80 [1.49-2.23]	1.93 [1.56-2.42]	1.85 [1.47-2.18]	1.77 [1.50-2.18]	1.72 [1.46-2.10]	0.006
Monocytes, 10^3 cells/µL	0.41 [0.32-0.53]	0.42 [0.32-0.55]	0.42 [0.32-0.54]	0.40 [0.33-0.51]	0.41 [0.32-0.52]	0.731
Eosinophils, 10^3 cells/µL	0.13 [0.09-0.20]	0.14 [0.09-0.21]	0.13 [0.09-0.19]	0.14 [0.09-0.24]	0.12 [0.09-0.19]	0.440
Basophils, 10^3 cells/µL	0.05 [0.03-0.07]	0.05 [0.03-0.07]	0.05 [0.03-0.07]	0.05 [0.03-0.07]	0.05 [0.03-0.06]	0.540

Data are presented as n (%) or median [Q1-Q3].
*hs-CRP= high-sensitivity C-reactive protein.

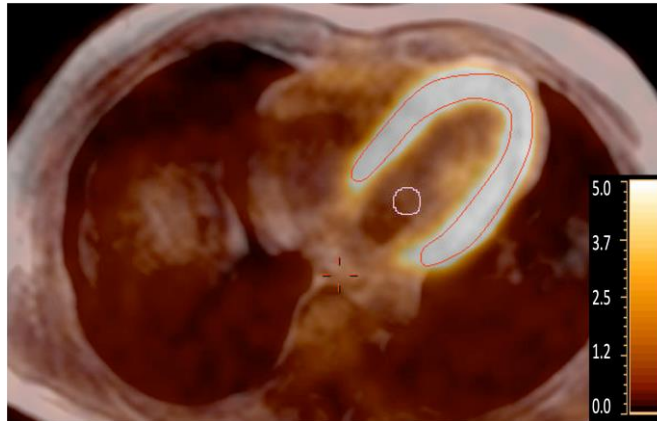**Supplementary Table 10. Progression of myocardial ^{18}F-FDG uptake according to changes in metabolic condition**

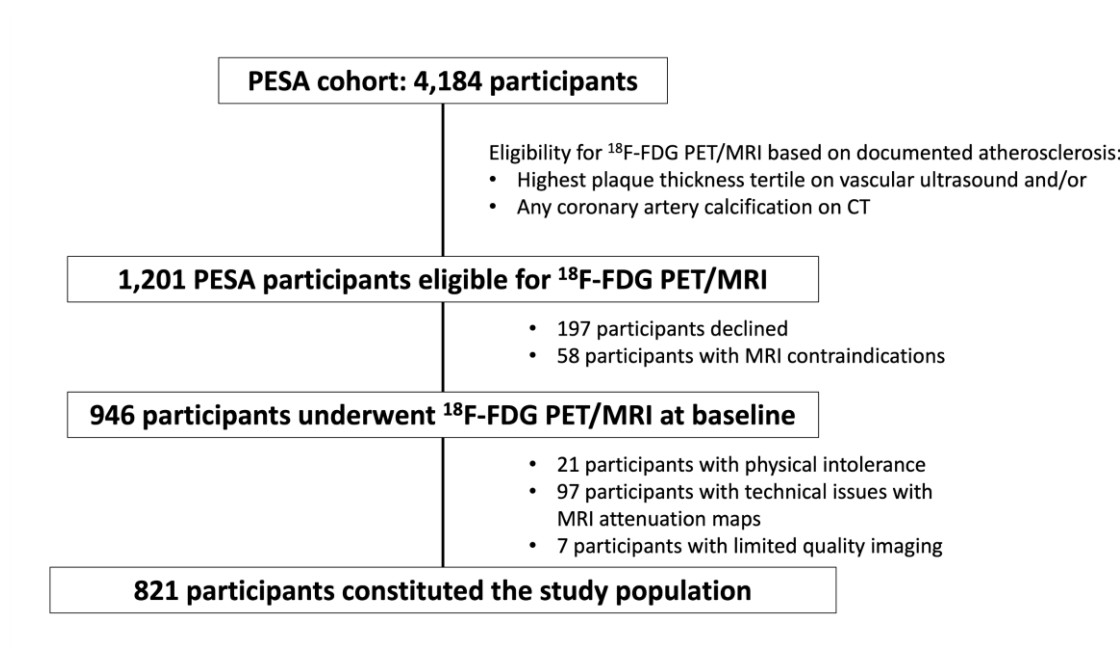|	n (%)*	TBRmax at Baseline PET-MR	TBRmax at follow-up PET-MR	p- value
No MetS	443 (75.9)	5.48	6.06	<0.001
MetS	46 (7.9)	4.30	3.81	0.340
MetS regression	45 (7.7)	2.70	5.33	<0.001
Onset of MetS	50 (8.6)	5.17	4.92	0.300

*data available in 584 participants

Supplementary Figures:

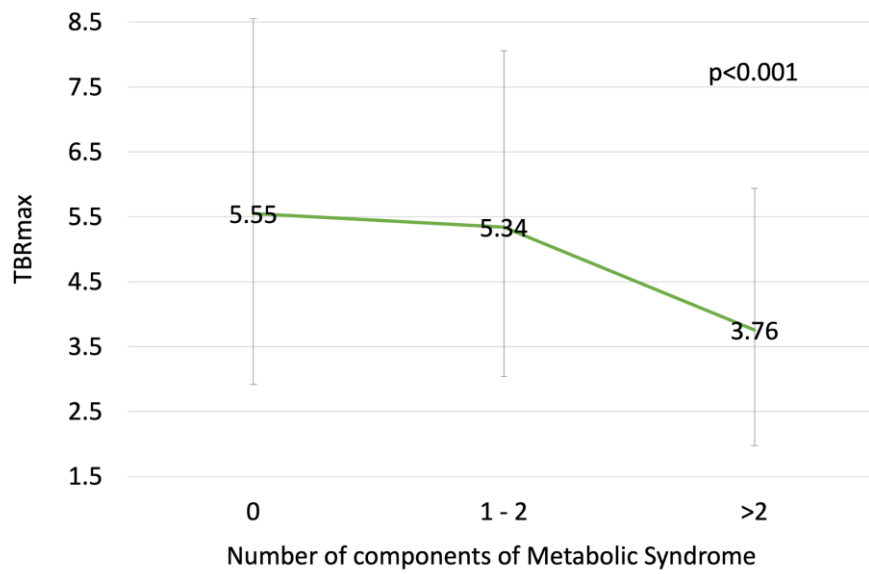**Supplementary Figure 1. Quantitative assessment of myocardial ^{18}F-FDG uptake**

Myocardial ^{18}F-FDG uptake was measured on fused PET-MR images of axial slices. Regions of interest were drawn in the myocardium and in the blood pool to obtain TBRmax.

Supplementary Figure 2: Study flowchart.

PESA cohort: 4,184 participants

Eligibility for ^{18}F-FDG PET/MRI based on documented atherosclerosis:
• Highest plaque thickness tertile on vascular ultrasound and/or
• Any coronary artery calcification on CT

1,201 PESA participants eligible for ^{18}F-FDG PET/MRI

• 197 participants declined
• 58 participants with MRI contraindications

946 participants underwent ^{18}F-FDG PET/MRI at baseline

• 21 participants with physical intolerance
• 97 participants with technical issues with MRI attenuation maps
• 7 participants with limited quality imaging

821 participants constituted the study population

Supplementary Figure 3: Myocardial ^{18}F-FDG uptake according to number of components of the Metabolic Syndrome.

	0 components	1-2 components	> 2 components	p trend
n	261	418	137	
TBRmax	5.55 [2.92-8.56]	5.34 [3.04-8.06]	3.76 [1.98-5.94]	<0.001