CIRCULATING MICRO-RNA PROFILES ACCORDING TO ATHEROSCLEROTIC DISEASE EXPRESSION. A CONTRIBUTE TO PHENOTYPE CHARACTERIZATION AND INSIGHTS INTO PATHOPHYSIOLOGY.

SUPPLEMENTARY MATERIALS

August, 2021

nms.unl.pt

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1. Preliminary exploratory analysis

The soluble CD40 ligand (sCD40L), tumor necrosis factor alpha (TNF-α), and vascular endothelial growth factor (VEGF) levels were quantified in a preliminary exploratory analysis. This included a subgroup consisting of the first 24 consecutive participants that were recruited. This analysis was performed with the aim of detecting trends in the expression levels of the aforementioned biomarkers, in order to decide if these biomarkers would be assessed in the whole recruited sample.

1.1. Characteristics of the participants

Table S1 presents the characteristics of participants included in the preliminary exploratory analysis.

Table S1. Characteristics of the participants in the preliminary exploratory analysis.

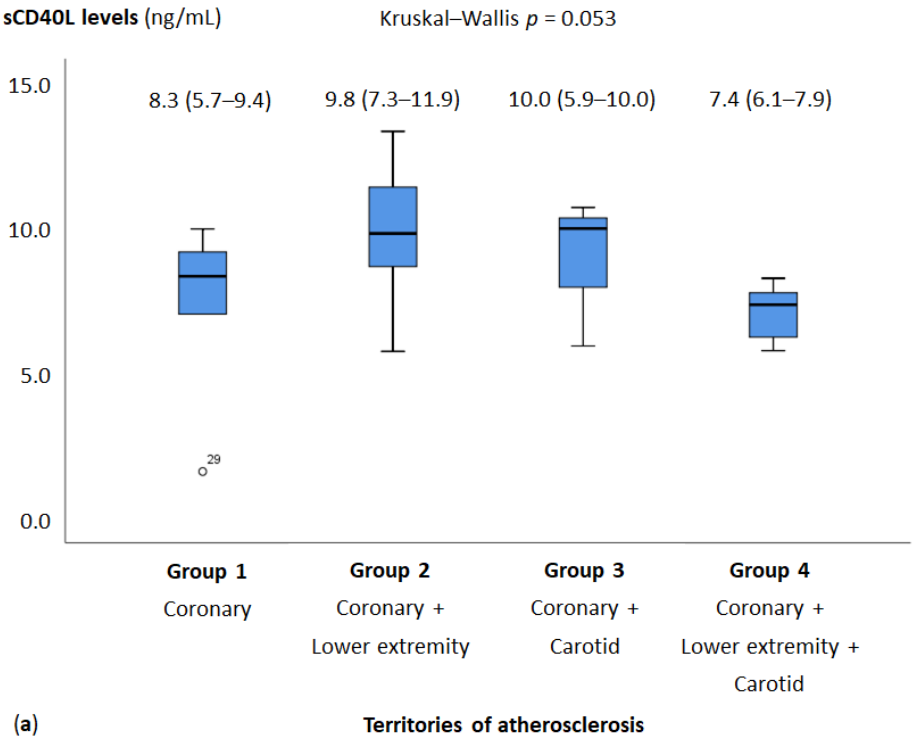
Study Group	**Group 1**	**Group 2**	**Group 3**	**Group 4**	***p*-value**
Territories of atherosclerosis	Coronary	Coronary + LE	Coronary + Carotid	Coronary + LE + Carotid	
n	6	9	3	6	
Clinical characteristics					
Age, years	62 (10)	66 (8)	59 (9)	87 (9)	0.397
Male, n (%)	6 (100.0)	8 (88.9)	2 (66.7)	5 (83.3)	0.308
Hypertension, n (%)	5 (83.3)	9 (100.0)	2 (66.7)	6 (100.0)	0.225
Dyslipidemia, n (%)	6 (100.0)	9 (100.0)	2 (66.7)	5 (83.3)	0.225
Diabetes mellitus, n (%)	3 (50.0)	4 (44.4)	1 (33.3)	5 (83.3)	0.397
Smoking history, n (%)	3 (50.0)	5 (55.6)	1 (33.3)	3 (50.0)	0.931
LVEF > 50%, n (%)	6 (100.0)	9 (100.0)	3 (100.0)	6 (100.0)	–
Antiplatelet therapy, n (%)	6 (100.0)	9 (100.0)	3 (100.0)	6 (100.0)	–
Statin therapy, n (%)	5 (83.3)	8 (88.9)	3 (100.0)	6 (100.0)	0.693
Laboratory parameters					
Hemoglobin, g/dL	14.7 (1.1)	14.2 (1.3)	11.3 (0.8) [a,b]	12.7 (1.0) [a,b]	<0.001
Leukocyte count, 10^9/L	7.6 (0.8)	8.2 (1.7)	8.5 (2.2)	8.5 (1.5)	0.811
Neutrophil count, 10^9/L	4.4 (1.2)	4.6 (1.7)	6.1 (1.5)	5.2 (1.6)	0.344

Lymphocyte count, 10^9/L	2.4 (0.7)	2.6 (1.2)	1.6 (0.7)	2.3 (0.4)	0.390
Neutrophil/lymphocyte ratio	1.0 (0.9–1.4)	0.8 (0.7–1.0)	1.3 (0.9–1.6)	0.9 (0.5–1.5)	0.546
Platelet count, 10^9/L	250 (41)	244 (36)	203 (75)	236 (29)	0.408
Fasting glycaemia, mg/dL	98 (83–189)	92 (83–148)	87 (67–87)	131 (107–183)	0.526
Percentage of glycosylated hemoglobin	6.3 (5.8–8.8)	5.7 (5.5–6.7)	5.4 (5.0–5.4)	7.9 (7.3–9.6) [b,c]	0.041
Creatinine, mg/dL	0.9 (0.9–1.1)	0.8 (0.7–1.1)	1.5 (0.8–1.5)	1.1 (0.8–1.5)	0.223
Total cholesterol, mg/dL	183 (38)	157 (28)	131 (49)	130 (33)	0.176
LDL-cholesterol, mg/dL	105 (31)	93 (21)	75 (35)	71 (26)	0.293
HDL-cholesterol, mg/dL	32 (4)	41 (12)	34 (8)	34 (10)	0.268
Triglycerides, mg/dL	174 (126–329)	109 (87–155)	63 (32–63)	110 (84–173)	0.063
C-reactive protein, mg/L	3.8 (1.5)	3.9 (1.2)	4.0 (2.2)	3.5 (1.5)	0.418
Coronary atherosclerosis					
Nr. of vessels with obstructive disease	3 (3–3)	3 (2–4)	3 (2–3)	3 (3–4)	0.811
Nr. of obstructive lesions	5 (4–5)	4 (4–5)	4 (3–4)	5 (4–5)	0.681
Gensini score	74 (34–120)	70 (40–110)	46 (40–77)	41 (33–77)	0.373
SYNTAX score	24.3 (12.4)	30.1 (10.9)	21.0 (1.7)	27.3 (7.5)	0.516
Prior CABG, n (%)	1 (16.7)	2 (22.2)	0 (0.0)	0 (0.0)	0.540
LE atherosclerosis					
Bilateral disease, n (%)	0 (0.0)	5 (55.6) [a,c]	0 (0.0)	5 (83.3) [a,c]	0.001
Any proximal lesion, n (%)	0 (0.0)	4 (44.4) [a,c]	0 (0.0)	4 (66.7) [a,c]	0.046
Nr. of segments with obstructive disease	0.0 (0.0)	2.8 (1.3) [a,c,d]	0.0 (0.0)	4.8 (0.8) [a–c]	<0.001
Prior bypass surgery, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	0.088
Carotid atherosclerosis					
Bilateral disease, n (%)	0 (0.0)	0 (0.0)	2 (66.7) [a,b]	4 (66.7) [a,b]	0.001

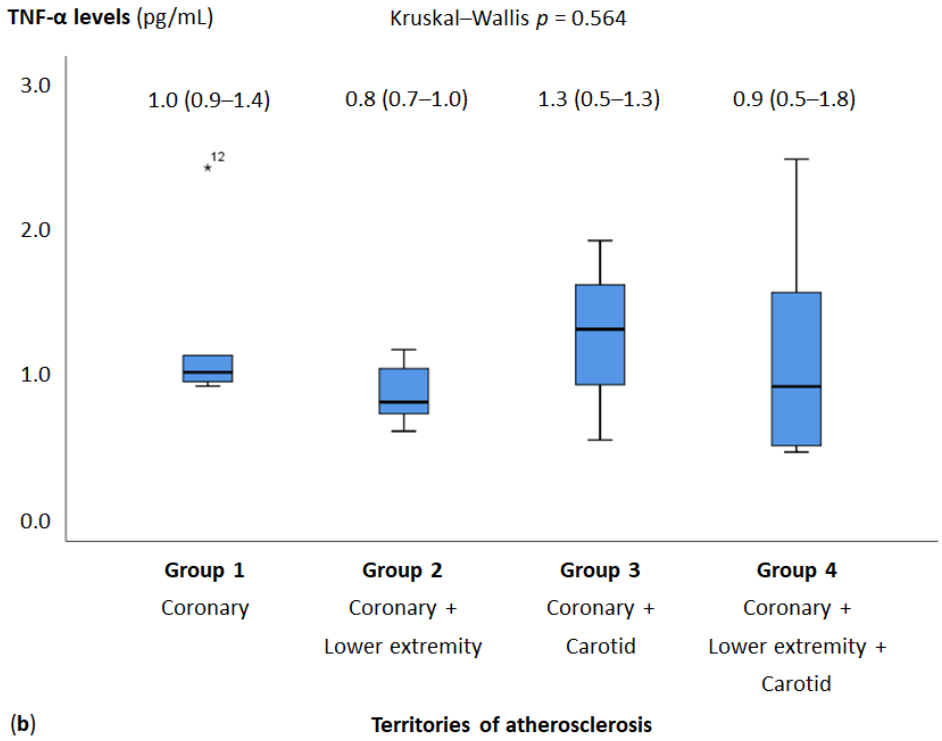
Categorical variables are expressed as frequency (percentage) and continuous variables as the mean (standard deviation) or median (interquartile range). CABG, coronary artery bypass grafting; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LE, lower extremity; LVEF, left ventricular ejection fraction; Nr., number; SYNTAX, SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery. [a] p-value < 0.05 vs. group 1; [b] p-value < 0.05 vs. group 2; [c] p-value < 0.05 vs. group 3; [d] p-value < 0.05 vs. group 4.

1.2. Expression levels of inflammatory and vascular biomarkers

Figure S1 presents the expression levels of inflammatory and vascular biomarkers. Only sCD40L levels showed a trend for differences according to the presence of single- and multi-territorial atherosclerosis.


sCD40L levels (ng/mL)
Kruskal–Wallis p = 0.053
15.0
10.0
5.0
0.0
8.3 (5.7–9.4)
9.8 (7.3–11.9)
10.0 (5.9–10.0)
7.4 (6.1–7.9)
29
Group 1
Coronary
Group 2
Coronary +
Lower extremity
Group 3
Coronary +
Carotid
Group 4
Coronary +
Lower extremity +
Carotid
Territories of atherosclerosis

(a)


TNF-α levels (pg/mL)
Kruskal–Wallis p = 0.564
3.0
2.0
1.0
0.0
1.0 (0.9–1.4)
0.8 (0.7–1.0)
1.3 (0.5–1.3)
0.9 (0.5–1.8)
12
Group 1
Coronary
Group 2
Coronary +
Lower extremity
Group 3
Coronary +
Carotid
Group 4
Coronary +
Lower extremity +
Carotid
Territories of atherosclerosis

(b)

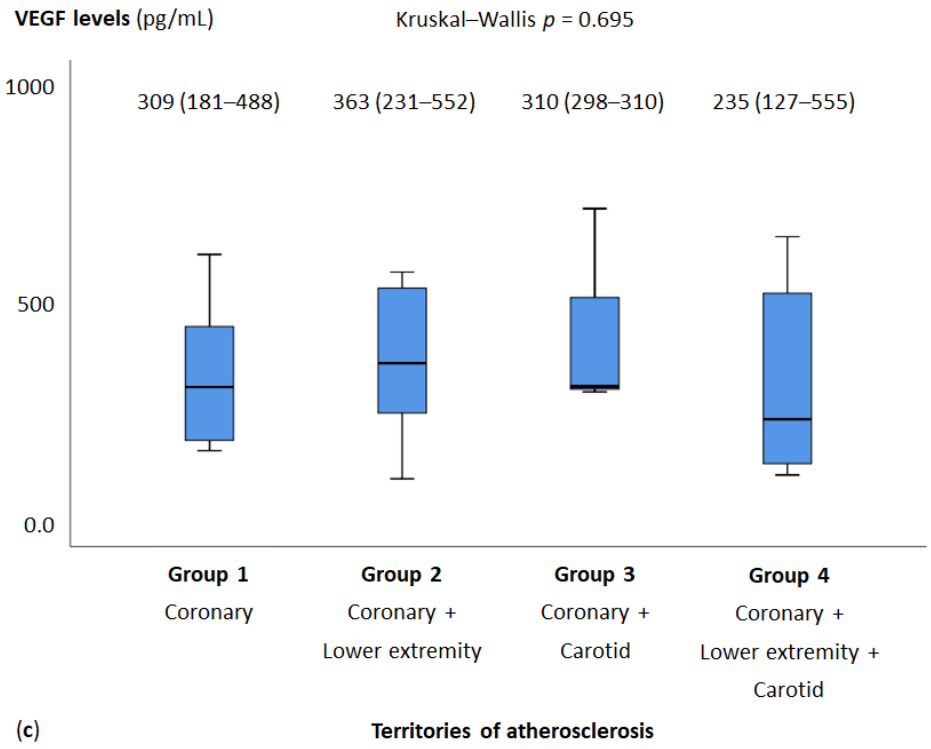


Figure S1. Levels of inflammatory and vascular biomarkers. Levels of (**a**) sCD40L, (**b**) TNF-α, and (**c**) VEGF are presented, and data are expressed as the median (interquartile range). sCD40L, soluble CD40 ligand; TNF-α, tumor necrosis factor alpha; VEGF, vascular endothelial growth factor.

Therefore, considering the estimated cost-effectiveness of measuring each biomarker in the entire sample, only sCD40L measurements were performed in the entire sample.

1.3. Parameters associated with miR-146a expression levels

The parameters associated with miR-146a expression levels in the preliminary exploratory analysis are presented in Table S2.

Table S2. Parameters associated with miR-146a expression levels in the preliminary exploratory analysis.

		ΔC_t miR-146a	***p*-value**
Clinical characteristics			
Age, years [a]		r = 0.085	0.738
Sex [b]	Male	22.2 (2.4)	0.117
	Female	25.1 (2.1)	
Hypertension [b]	No	21.6 (2.5)	0.711
	Yes	22.6 (2.5)	
Dyslipidemia [b]	No	21.8 (2.4)	0.701
	Yes	22.5 (2.5)	
Diabetes mellitus [b]	No	22.4 (2.1)	0.827
	Yes	22.6 (2.8)	
Smoking history [b]	No	22.6 (2.6)	0.865
	Yes	22.3 (2.2)	
Left ventricular ejection fraction [b]	≤ 50%	–	–
	> 50%	22.5 (2.5)	
Antiplatelet therapy [b]	No	–	–
	Yes	22.5 (2.5)	
Statin therapy [b]	No	21.3 (2.5)	0.618
	Yes	22.6 (2.5)	
Laboratory data			
Hemoglobin, g/dL [a]		r = -0.488	0.040
Leukocyte count, 10^9/L [a]		r = -0.090	0.723
Neutrophil count, 10^9/L [a]		r = -0.270	0.279
Lymphocyte count, 10^9/L [a]		r = 0.271	0.277
Neutrophil/lymphocyte ratio [a]		r = -0.231	0.357
Platelet count, 10^9/L [a]		r = 0.263	0.292
Fasting glycaemia, mg/dL [a]		r = 0.371	0.129
Percentage of glycosylated hemoglobin [a]		r = 0.317	0.200
Creatinine, mg/dL [a]		r = 0.337	0.171
Total cholesterol, mg/dL [a]		r = 0.280	0.260
LDL-cholesterol, mg/dL [a]		r = -0.058	0.820
HDL-cholesterol, mg/dL [a]		r = 0.294	0.236
Triglycerides, mg/dL [a]		r = 0.029	0.908

Soluble CD40 ligand, ng/mL [a]	r = 0.312	0.236
Vascular endothelial growth factor, pg/mL [a]	r = 0.304	0.220
C-reactive protein, mg/L [a]	r = 0.304	0.207

[a] Correlations between miR-146a expression levels (ΔC_t) and continuous variables were tested and the correlation coefficient (r) is presented for each; [b] miR-146a expression levels (ΔC_t) were compared between groups for categorical variables and are expressed as the mean (standard deviation) or median (interquartile range). HDL, high-density lipoprotein; LDL, low-density lipoprotein; ΔC_t, delta cycle threshold.

2. Parameters associated with the expression levels of miR-27b and miR-146a in univariate analysis

The parameters associated with ΔC_t miR-27b and ΔC_t miR-146a in the univariate analysis are presented in Tables S3 and S4, respectively.

Table S3. Association of clinical characteristics, laboratory results, and atherosclerosis data with miR-27b expression levels.

		ΔC_t miR-27b	***p*-value**
Clinical data			
Age, years [a]		r = 0.137	0.254
Sex [b]	Male	19.4 (15.16–23.11)	0.585
	Female	17.88 (13.63–23.24)	
Hypertension [b]	No	19.77 (15.81–22.16)	1.000
	Yes	18.71 (14.96–23.53)	
Dyslipidemia [b]	No	19.93 (15.73–21.26)	0.649
	Yes	18.35 (14.97–23.79)	
Diabetes mellitus [b]	No	18.29 (15.75–22.12)	0.377
	Yes	22.09 (14.41–24.10)	
Smoking history [b]	No	19.29 (4.42)	0.892
	Yes	19.15 (4.34)	
Antiplatelet therapy [b]	No	17.03 (14.05–19.85)	0.014
	Yes	20.71 (16.18–23.89)	
Statin therapy [b]	No	17.89 (14.53–20.10)	0.118
	Yes	19.50 (15.33–23.83)	
Laboratory data			
Hemoglobin, g/dL [a]		r = -0.200	0.097
Leukocyte count, 10^9/L [a]		r = 0.197	0.111
Neutrophil count, 10^9/L [a]		r = 0.188	0.122
Lymphocyte count, 10^9/L [a]		r = 0.081	0.512
Neutrophil/lymphocyte ratio [a]		r = 0.132	0.286
Platelet count, 10^9/L [a]		r = 0.185	0.132
Fasting glycaemia, mg/dL [a]		r = 0.023	0.849
Percentage of glycosylated hemoglobin [a]		r = 0.128	0.311
Creatinine, mg/dL [a]		r = 0.283	0.017
Total cholesterol, mg/dL [a]		r = -0.068	0.578

LDL-cholesterol, mg/dL [a]		r = -0.033	0.788
HDL-cholesterol, mg/dL [a]		r = -0.123	0.312
Triglycerides, mg/dL [a]		r = -0.041	0.737
C-reactive protein, mg/L [a]		r = 0.018	0.889
Atherosclerosis data			
Coronary atherosclerosis			
Nr. of vessels with obstructive disease [a]		r = 0.241	0.043
Nr. of obstructive lesions [a]		r = 0.241	0.043
Gensini score [a]		r = 0.147	0.221
SYNTAX score [a]		r = 0.286	0.019
Prior coronary artery bypass grafting [b]	No	20.68 (18.16–21.22)	0.301
	Yes	18.89 (16.27–19.04)	
LE atherosclerosis			
Nr. of sides affected [b]	One	20.32 (15.11–23.22)	0.041
	Two	24.01 (17.18–25.72)	
Any proximal lesion [b]	No	18.32 (15.66–22.39)	0.294
	Yes	22.32 (14.97–24.06)	
Nr. of segments with obstructive disease [a]		r = 0.320	0.008
Prior bypass surgery [b]	No	21.90 (15.51–23.92)	0.498
	Yes	22.06 (16.50–24.34)	
Carotid atherosclerosis			
Nr. of sides affected [b]	One	19.89 (13.31–24.51)	0.857
	Two	23.41 (17.17–24.49)	
Mean IMT, mm [a]		r = -0.125	0.481
Maximal IMT, mm [a]		r = -0.072	0.704

[a] Correlations between miR-27b expression levels (ΔC_t miR-27b) and continuous variables were tested and the correlation coefficient (r) is presented for each; [b] miR-27b expression levels (ΔC_t miR-27b) were compared between groups for categorical variables and are expressed as the mean (standard deviation) or median (interquartile range). Higher ΔC_t miR-27b represent lower circulating levels of miR-27b. HDL, high-density lipoprotein; IMT, intima–media thickness; LDL, low-density lipoprotein; LE, lower extremity; Nr., number; SYNTAX, SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery; ΔC_t, delta cycle threshold.

Table S4. Association of clinical characteristics, laboratory results, and atherosclerosis data with miR-146a expression levels.

		ΔC_t miR-146a	***p*-value**
Clinical data			
Age, years [a]		r = 0.139	0.234
Sex [b]	Male	19.46 (3.75)	0.643
	Female	18.79 (4.54)	
Hypertension [b]	No	19.60 (2.87)	0.833
	Yes	19.35 (3.99)	
Dyslipidemia [b]	No	19.69 (2.71)	0.814
	Yes	19.35 (3.94)	
Diabetes mellitus [b]	No	19.09 (3.59)	0.357
	Yes	19.95 (4.21)	
Smoking history [b]	No	19.65 (3.61)	0.528
	Yes	19.09 (4.06)	
Antiplatelet therapy [b]	No	17.64 (2.91)	0.031
	Yes	19.90 (3.92)	
Statin therapy [b]	No	18.92 (3.67)	0.434
	Yes	19.72 (3.58)	
Laboratory data			
Hemoglobin, g/dL [a]		r = -0.140	0.236
Leukocyte count, 10^9/L [a]		r = 0.161	0.178
Neutrophil count, 10^9/L [a]		r = 0.169	0.154
Lymphocyte count, 10^9/L [a]		r = 0.031	0.794
Neutrophil/lymphocyte ratio [a]		r = 0.157	0.192
Platelet count, 10^9/L [a]		r = 0.201	0.091
Fasting glycaemia, mg/dL [a]		r = 0.071	0.550
Percentage of glycosylated hemoglobin [a]		r = 0.179	0.142
Creatinine, mg/dL [a]		r = 0.202	0.082
Total cholesterol, mg/dL [a]		r = -0.079	0.505
LDL-cholesterol, mg/dL [a]		r = -0.043	0.713
HDL-cholesterol, mg/dL [a]		r = -0.039	0.741
Triglycerides, mg/dL [a]		r = -0.080	0.501
C-reactive protein, mg/L [a]		r = -0.100	0.419
Atherosclerosis data			
Coronary atherosclerosis			
Nr. of vessels with obstructive disease [a]		r = 0.242	0.036
Nr. of obstructive lesions [a]		r = 0.289	0.012
Gensini score [a]		r = 0.067	0.569

SYNTAX score [a]		r = 0.257	0.037
Prior coronary artery bypass grafting [b]	No	20.97 (16.94–22.80)	0.209
	Yes	18.34 (15.74–20.81)	
LE atherosclerosis			
Nr. of sides affected [b]	One	18.84 (16.37–22.34)	0.068
	Two	21.98 (19.46–25.11)	
Any proximal lesion [b]	No	19.18 (3.48)	0.161
	Yes	20.53 (3.88)	
Nr. of segments with obstructive disease [a]		r = 0.352	0.003
Prior bypass surgery [b]	No	20.13 (4.17)	0.437
	Yes	21.59 (4.55)	
Carotid atherosclerosis			
Nr. of sides affected [b]	One	19.58 (4.95)	0.352
	Two	21.40 (3.18)	
Mean IMT, mm [a]		r = -0.133	0.438
Maximal IMT, mm [a]		r = -0.028	0.878

[a] Correlations between miR-146a expression levels (ΔC_t miR-146a) and continuous variables were tested and the correlation coefficient (r) is presented for each; [b] miR-146a expression levels (ΔC_t miR-146a) were compared between groups for categorical variables and are expressed as the mean (standard deviation) or median (interquartile range). Higher ΔC_t miR-146a represent lower circulating levels of miR-146a. HDL, high-density lipoprotein; IMT, intima–media thickness; LDL, low-density lipoprotein; LE, lower extremity; Nr., number; SYNTAX, SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery; ΔC_t, delta cycle threshold.

3. Parameters associated with the Gensini score in univariate analysis

The univariate analysis with clinical and laboratory parameters associated with the Gensini score, as a continuous variable, is presented in Table S5.

Table S5. Parameters associated with the Gensini score in univariate analysis.

		Gensini score	*p*-value
Clinical parameters			
Age, years [a]		r = 0.201	0.053
Sex [b]	Male	53.6 (49.9)	0.877
	Female	45.3 (39.4)	
Hypertension [b]	No	25.9 (53.4)	0.002
	Yes	58.2 (46.2)	
Dyslipidemia [b]	No	12.4 (32.2)	0.001
	Yes	58.1 (48.2)	
Diabetes mellitus [b]	No	49.1 (51.4)	0.170
	Yes	59.7 (43.1)	
Smoking history [b]	No	54.5 (53.3)	0.105
	Yes	48.4 (36.2)	
Antiplatelet therapy [b]	No	7.7 (16.7)	<0.001
	Yes	66.5 (45.7)	
Statin therapy [b]	No	17.9 (24.9)	<0.001
	Yes	60.7 (47.7)	
Laboratory parameters			
Hemoglobin, g/dL [a]		r = 0.066	0.530
Leukocyte count, 10^9/L [a]		r = 0.294	0.005
Neutrophil count, 10^9/L [a]		r = 0.265	0.011
Lymphocyte count, 10^9/L [a]		r = 0.000	0.999
Neutrophil/lymphocyte ratio [a]		r = 0.309	0.003
Platelet count, 10^9/L [a]		r = -0.048	0.650
Fasting glycaemia, mg/dL [a]		r = 0.031	0.771
Percentage of glycosylated hemoglobin [a]		r = 0.044	0.689
Creatinine, mg/dL [a]		r = 0.322	0.002
Total cholesterol, mg/dL [a]		r = -0.149	0.156
LDL-cholesterol, mg/dL [a]		r = -0.064	0.543

HDL-cholesterol, mg/dL [a]	r = -0.450	<0.001
Triglycerides, mg/dL [a]	r = 0.064	0.545
C-reactive protein, mg/L [a]	r = 0.066	0.549
sCD40L, ng/mL [a]	r = 0.279	0.007

[a] Correlations between the Gensini score and continuous variables were tested and the correlation coefficient (r) is presented for each; [b] the Gensini score was compared between groups for categorical variables and is expressed as the mean (standard deviation). HDL, high-density lipoprotein; LDL, low-density lipoprotein; sCD40L, soluble CD40 ligand.

4. Parameters associated with soluble CD40 ligand levels in univariate analysis

The parameters associated with sCD40L levels in the univariate analysis are presented in Table S6.

Table S6. Association of soluble CD40 ligand levels with clinical characteristics, laboratory results, and atherosclerosis data.

		sCD40L, ng/mL	*p*-value
Clinical data			
Age, years [a]		r = -0.085	0.419
Sex [b]	Male	4.2 (2.7–8.8)	0.876
	Female	5.1 (2.9–7.2)	
Hypertension [b]	No	4.3 (2.9–6.0)	0.555
	Yes	5.1 (2.9–7.6)	
Dyslipidemia [b]	No	5.2 (2.7–7.0)	0.953
	Yes	5.0 (2.9–7.6)	
Diabetes mellitus [b]	No	5.0 (3.2–7.3)	0.555
	Yes	4.8 (2.3–7.6)	
Smoking history [b]	No	4.2 (2.8–7.1)	0.363
	Yes	5.9 (2.9–7.8)	
Antiplatelet therapy [b]	No	3.9 (2.8–5.3)	0.139
	Yes	5.5 (3.1–7.9)	
Statin therapy [b]	No	4.4 (2.5–5.3)	0.115
	Yes	5.1 (3.0–7.7)	
Laboratory data			
Hemoglobin, g/dL [a]		r = 0.123	0.243
Leukocyte count, 10^9/L [a]		r = 0.301	0.004
Neutrophil count, 10^9/L [a]		r = 0.219	0.037
Lymphocyte count, 10^9/L [a]		r = 0.292	0.005
Neutrophil/lymphocyte ratio [a]		r = -0.041	0.704
Platelet count, 10^9/L [a]		r = 0.223	0.035
Fasting glycaemia, mg/dL [a]		r = 0.114	0.284
Percentage of glycosylated hemoglobin [a]		r = 0.136	0.217
Creatinine, mg/dL [a]		r = 0.118	0.258
Total cholesterol, mg/dL [a]		r = -0.017	0.874

LDL-cholesterol, mg/dL [a]		r = 0.014	0.897
HDL-cholesterol, mg/dL [a]		r = -0.222	0.036
Triglycerides, mg/dL [a]		r = 0.039	0.717
C-reactive protein, mg/L [a]		r = 0.095	0.388
Atherosclerosis data			
Coronary atherosclerosis			
Nr. of vessels with obstructive disease [a]		r = 0.285	0.006
Nr. of obstructive lesions [a]		r = 0.238	0.022
Gensini score [a]		r = 0.279	0.007
SYNTAX score [a]		r = 0.265	0.015
Prior coronary artery bypass grafting [b]	No	6.8 (3.5)	0.001
	Yes	4.3 (2.1)	
LE atherosclerosis			
Nr. of sides affected [b]	One	6.0 (4.0)	0.822
	Two	5.8 (3.0)	
Any proximal lesion [b]	No	7.3 (3.7)	0.101
	Yes	5.3 (3.0)	
Nr. of segments with obstructive disease [a]		r = 0.157	0.147
Prior bypass surgery [b]	No	6.8 (3.5)	0.036
	Yes	3.9 (2.5)	
Carotid atherosclerosis			
Nr. of sides affected [b]	One	5.2 (3.1)	0.083
	Two	5.7 (2.7)	
Mean IMT, mm [a]		r = -0.200	0.215
Maximal IMT, mm [a]		r = -0.169	0.271

[a] Correlations between soluble CD40 ligand levels and continuous variables were tested and the correlation coefficient (r) is presented for each; [b] soluble CD40 ligand levels were compared between groups for categorical variables and are expressed as the mean (standard deviation) or median (interquartile range). Each tested association under the heading of the respective territory of disease (coronary, lower extremity, and carotid) included only patients with obstructive disease of the corresponding territory, with the exception of intima–media thickness, which only included participants without obstructive carotid atherosclerosis. HDL, high-density lipoprotein; IMT, intima–media thickness; LDL, low-density lipoprotein; LE, lower extremity; Nr., number; sCD40L, soluble CD40 ligand; SYNTAX, SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery.

5. Characteristics of participants without and with prior revascularization

5.1. Participants without and with prior coronary artery bypass grafting

The characteristics of participants without and with prior coronary artery bypass grafting are presented in Table S7.

Table S7. Characteristics of participants with coronary atherosclerosis, without and with prior coronary artery bypass grafting.

	No prior CABG	**Prior CABG**	***p*-value**
n	45	23	
Clinical characteristics			
Age, years	64.9 (10.2)	64.7 (7.3)	0.645
Male, n (%)	41 (91.1)	20 (87.0)	0.681
Hypertension, n (%)	43 (95.6)	21 (91.3)	0.599
Dyslipidemia, n (%)	42 (93.3)	23 (100.0)	0.546
Diabetes mellitus, n (%)	20 (44.4)	9 (39.1)	0.675
Smoking history, n (%)	26 (57.8)	11 (47.8)	0.436
Left ventricular ejection fraction > 50%, n (%)	45 (100.0)	23 (100.0)	–
Antiplatelet therapy, n (%)	43 (95.6)	23 (100.0)	0.546
Statin therapy, n (%)	40 (88.9)	21 (91.3)	1.000
Laboratory parameters			
Hemoglobin, g/dL	13.6 (1.5)	13.7 (1.8)	0.780
Leukocyte count, 10^9/L	8.0 (1.8)	6.7 (1.6)	0.003
Neutrophil count, 10^9/L	4.8 (1.4)	3.8 (1.7)	0.001
Lymphocyte count, 10^9/L	2.2 (0.9)	1.8 (0.7)	0.133
Neutrophil/lymphocyte ratio	2.4 (1.0)	2.3 (1.1)	0.457
Platelet count, 10^9/L	234 (49)	200 (48)	0.011
Fasting glycaemia, mg/dL	114 (50)	111 (58)	0.892
Percentage of glycosylated hemoglobin	6.6 (1.5)	6.1 (1.3)	0.171
Creatinine, mg/dL	1.1 (0.4)	1.0 (0.3)	0.367
Total cholesterol, mg/dL	171 (43)	158 (52)	0.274
LDL-cholesterol, mg/dL	104 (36)	94 (42)	0.291
HDL-cholesterol, mg/dL	38 (9)	38 (10)	0.859

Triglycerides, mg/dL	156 (58)	136 (52)	0.169
C-reactive protein, mg/L	3.6 (1.3)	3.8 (1.9)	0.611
Coronary atherosclerosis			
Nr. of vessels with obstructive disease	3.0 (0.9)	2.8 (0.7)	0.438
Nr. of obstructive lesions	4.1 (1.2)	3.8 (1.6)	0.243
Gensini score	71 (36)	76 (54)	0.928
SYNTAX score	25.8 (8.5)	28.4 (11.4)	0.338
LE atherosclerosis			
Presence of LE arterial disease, n (%)	26 (57.8)	10 (43.5)	0.311
Bilateral disease, n (%)	20 (44.4)	5 (21.7)	0.150
Any proximal lesion, n (%)	15 (33.3)	7 (30.4)	1.000
Nr. of segments with obstructive disease	1.9 (1.1)	1.5 (0.9)	0.256
Prior bypass surgery, n (%)	5 (11.1)	3 (13.0)	1.000
Carotid atherosclerosis			
Presence of carotid artery disease, n (%)	21 (46.7)	9 (39.1)	0.613
Bilateral disease, n (%)	9 (20.0)	2 (8.7)	0.488
Mean IMT, mm	0.70 (0.08)	0.73 (0.09)	0.763
Maximal IMT, mm	0.90 (0.09)	0.92 (0.12)	0.857

Data are expressed as the mean (standard deviation), except if otherwise specified. CABG, coronary artery bypass grafting; HDL, high-density lipoprotein; IMT, intima–media thickness; LDL, low-density lipoprotein; LE, lower extremity; Nr., number; sCD40L, soluble CD40 ligand; SYNTAX, SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery.

5.2. Participants without and with prior lower extremity bypass surgery

The characteristics of participants without and with prior lower extremity bypass surgery are presented in Table S8.

Table S8. Characteristics of participants with lower extremity atherosclerosis, without and with prior lower extremity bypass surgery.

	No prior LE bypass surgery	**Prior LE bypass surgery**	***p*-value**
n	28	8	
Clinical characteristics			
Age, years	67 (8.5)	67 (7.0)	0.887
Male, n (%)	26 (92.9)	7 (87.5)	0.541
Hypertension, n (%)	28 (100.0)	8 (100.0)	–
Dyslipidemia, n (%)	27 (96.4)	8 (100.0)	1.000
Diabetes mellitus, n (%)	12 (42.9)	5 (62.5)	0.281
Smoking history, n (%)	18 (64.3)	6 (75.0)	0.691
LVEF > 50%, n (%)	28 (100.0)	8 (100.0)	–
Antiplatelet therapy, n (%)	27 (96.4)	8 (100.0)	1.000
Statin therapy, n (%)	25 (89.3)	7 (87.5)	0.553
Laboratory parameters			
Hemoglobin, g/dL	13.8 (1.5)	12.9 (1.7)	0.193
Leukocyte count, 10^9/L	7.8 (1.6)	7.1 (2.1)	0.288
Neutrophil count, 10^9/L	4.1 (3.4–5.5)	3.9 (2.5–5.9)	0.762
Lymphocyte count, 10^9/L	2.4 (0.8)	1.8 (0.5)	0.101
Neutrophil/lymphocyte ratio	2.1 (0.9)	2.6 (1.3)	0.304
Platelet count, 10^9/L	225 (44)	235 (49)	0.620
Fasting glycaemia, mg/dL	87 (79–121)	106 (85–160)	0.229
Percentage of glycosylated hemoglobin	5.9 (5.5–7.1)	5.5 (5.0–9.6)	0.439
Creatinine, mg/dL	0.9 (0.8–1.3)	1.3 (1.0–1.6)	0.083
Total cholesterol, mg/dL	172 (46)	174 (63)	0.918
LDL-cholesterol, mg/dL	109 (38)	111 (44)	0.610
HDL-cholesterol, mg/dL	37 (30–42)	35 (34–46)	0.793
Triglycerides, mg/dL	117 (89–173)	163 (87–203)	0.558
C-reactive protein, mg/L	3.4 (1.9)	3.8 (2.1)	0.611
Coronary atherosclerosis			
Presence of coronary artery disease, n (%)	28 (100.0)	8 (100.0)	–
Nr. of vessels with obstructive disease	3 (3–4)	3 (2-4)	0.284
Nr. of obstructive lesions	4 (3–5)	4 (3–5)	0.668
Gensini score	78 (39–116)	49 (24–46)	0.101
SYNTAX score	28.2 (9.4)	31.8 (14.3)	0.480
Prior CABG, n (%)	7 (25.0)	3 (37.5)	0.658
LE atherosclerosis			
Bilateral disease, n (%)	18 (64.3)	7 (87.5)	0.201
Any proximal lesion, n (%)	15 (53.4)	7 (87.5)	0.218

Nr. of segments with obstructive disease	2.8 (1.6)	4.1 (1.8)	0.064
Carotid atherosclerosis			
Presence of carotid artery disease, n (%)	12 (42.9)	6 (75.9)	0.638
Bilateral disease, n (%)	6 (21.4)	2 (25.0)	0.207
Mean IMT, mm	0.77 (0.06)	0.75 (0.07)	0.463
Maximal IMT, mm	0.95 (0.09)	0.92 (0.10)	0.457

Categorical variables are expressed as frequency (percentage) and continuous variables as the mean (standard deviation) or median (interquartile range). CABG, coronary artery bypass grafting; HDL, high-density lipoprotein; IMT, intima–media thickness; LDL, low-density lipoprotein; LE, lower extremity; LVEF, left ventricular ejection fraction; Nr., number; SYNTAX, SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery.