Supplementary Material

Table S1. Characteristics of the study cohort according with risk factor (RF) categorization.

Parameter	Low RF (n=322)	Multiple RF (n=222)	*p*-value
Age, years	59.3 ± 8.6	60.2 ± 7.9	0.210
Sex, male	195 (60.6)	123 (55.4)	0.231
BMI, kg/m^2	25.8 ± 4.0	27.8 ± 4.3	1.5×10^{-7}
Family history of CAD, yes	32 (9.9)	137 (61.7)	1.2×10^{-37}
Hypertension, yes	91 (28.3)	196 (88.3)	3.2×10^{-43}
Current smoker, yes	23 (7.1)	110 (49.5)	1.2×10^{-29}
Diabetes, yes	0 (0.0)	68 (30.6)	2.5×10^{-26}
Systolic BP, mmHg	126.7 ± 14.6	131.9 ± 15.8	7.9×10^{-5}
Antiplatelets, yes	56 (17.4)	89 (40.1%)	4.0×10^{-9}
Statins, yes	29 (9.0)	141 (63.5%)	2.0×10^{-41}
Total-c, mg/dL	202.1 ± 41.5	210.9 ± 47.9	0.127
LDL-c, mg/dL	126.4 ± 39.1	132.7 ± 44.5	0.237
HDL-c, mg/dL	58.6 ± 20.1	51.3 ± 15.2	0.003
Triglycerides, mg/dL	91 [65 – 135]	139 [97 – 207]	7.1×10^{-8}
Serum creatinine, mg/dL	0.86 ± 0.18	0.86 ± 0.19	0.907
OPN, ng/mL	20.3 [14.8 – 27.0]	19.6 [14.5 – 27.5]	0.844
MPO, ng/mL	99.3 [56.6 – 186.3]	140.8 [78.2 – 283.6]	4.0×10^{-6}
Resistin, ng/mL	13.3 [9.4 – 19.0]	13.9 [10.3 – 20.3]	0.101

Continuous data are presented as mean ±SD or median [interquartile range], according with their distribution. Categorical data are presented as absolute (relative) frequencies. P-value for one-way ANOVA, Mann-Whitney or χ2 tests, as appropriate. RF: risk factors; BMI: body mass index; CAD: coronary artery disease; BP: blood pressure; total-c: total cholesterol; LDL-c: low-density lipoprotein cholesterol; HDL-c: high-density lipoprotein cholesterol; OPN: osteopontin; MPO: myeloperoxidase.

Table S2. Association between serum levels of osteopontin (OPN) and coronary atherosclerotic plaque extent/severity in coronary artery disease (CAD) groups (low/high risk factors).

	OPN (ng/mL)	p-value
CAD extent		
<7 segments affected (n=91)	22.2 [16.6 – 29.7]	0.859
>7 segments affected (n=102)	22.8 [14.6 – 29.8]	
CAD severity		
No segment >50% affected (n=182)	22.6 [15.7 – 29.8]	0.210
Any segment >50% affected (n=10)	18.1 [10.5 – 29.8]	
Plaque composition		
>50% non-calcified (n=11)	23.4 [13.8 – 30.3]	
>50% calcified (n=130)	23.0 [16.7 – 30.6]	0.265
Mixed (n=53)	19.9 [13.9 – 27.8]	

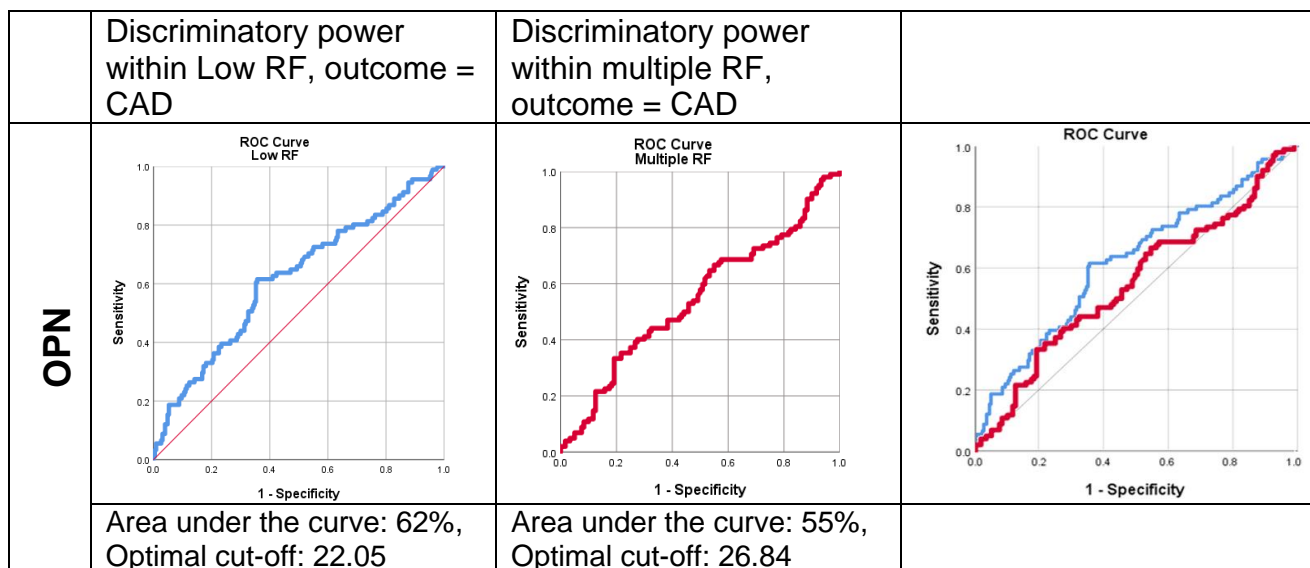P-value for one-way ANOVA or Mann-Whitney tests, as appropriate.

Figure S1. ROC curve analysis testing the predictive role of osteopontin (OPN), toward the presence of coronary artery disease according with risk factor categorization.

	Discriminatory power within Low RF, outcome = CAD	Discriminatory power within multiple RF, outcome = CAD	
OPN			
	Area under the curve: 62%, Optimal cut-off: 22.05	Area under the curve: 55%, Optimal cut-off: 26.84	

Figure S1. ROC curve analyses. ROC curve analyses testing the accuracy of osteopontin (OPN) toward the presence of coronary artery disease (CAD) according with risk factor (RF) categorization.

Appendix

Steering Committee

A. Maseri † (Chairman; Firenze), D. Andreini (Milano), S. Berti (Massa), M. Canestrari (Fano), G. Casolo (Lido di Camaiore), D. Gabrielli (Roma), R. Latini (Milano), M. Magnoni (Milano), P. Marraccini (Pisa), T. Moccetti (Lugano), M.G. Modena (Modena)

Coordinating Center: A.P. Maggioni, M. Gorini, F. Bianchini, I. Cangioli, A. Lorimer (Centro Studi ANMCO Firenze)

Imaging Core Laboratory: D. Andreini, G. Pontone, E. Conte (Centro Cardiologico Monzino Milano)

Centralized biobank and biomarker core laboratory: D. Novelli, F. Gaspari, S. Ferrari, A. Cannata, N. Stucchi, M. Fois, R. Bernasconi, G. Balconi (Istituto Mario Negri, Milano and Bergamo), T. Vago, T. Letizia (Ospedale Luigi Sacco, Milano), B. Bottazzi, R. Leone (Istituto Clinico Humanitas, Rozzano).

Central ECG Reading: I. Suliman (Centro Studi ANMCO, Firenze)

Psychologists CRF Group: M. Sommaruga † (IRCCS Salvatore Maugeri Unità di Psicologia, Milano), P. Gremigni (Dipartimento di Psicologia Università di Bologna)

Participating Centers and Investigators

Fano, Ospedale S Croce (R. Olivieri); Fermo, Ospedale Civile A. Murri (L. Pennacchietti); Lido di Camaiore, Nuovo Ospedale Versilia (M. Magnacca); Lugano, Cardiocentro Ticino (M.G. Rossi, E. Pasotti, T. Moccetti); Massa, FTGM - Stabilimento di Massa (A. Clemente); Milano, Centro Cardiologico Monzino (D. Andreini, G. Pontone, S. Mushtaq); Modena, Ospedale Policlinico (E. Mauro, G. Boriani); Parma, AOU. di Parma (F. Pigazzani); Pisa, AOU Pisana (L. Faggioni); Pisa, FTGM - Stabilimento di Pisa (M. Ciardetti); Udine, AOU SM della Misericordia (M. Puppato