Supplementary material

Evaluation metrics

1. $TP = \sum_{i=1}^{N} \left(\hat{y}_i = 1 \mid y_i = 1 \right)$
2. $FP = \sum_{i=1}^{N} \left(\hat{y}_i = 1 \mid y_i = 0 \right)$
3. $TN = N_n - FP$
4. $FN = N_p - TP$
5. $Logloss = -\frac{1}{N} \sum_{i=1}^{N} \left[y_i \ln p_i + \left(1 - y_i\right) \ln \left(1 - p_i\right) \right]$
6. $Accuracy = \frac{TP + TN}{TP + TN + FP + FN}$
7. $Precision = \frac{TP}{TP + FP}$
8. $Recall \,/\, Sensitivity = \frac{TP}{TP + FN}$
9. $F1 = 2 * \frac{Precision * Recall}{Precision + Recall}$
10. $Specificity = \frac{TN}{TN + FP}$

Abbreviations:
y : the actual/true value,
$\hat{y}$: the predicted value,
p : the predicted probability for a sample to belong in positive class,
ln : the natural logarithm,
N : the number of samples (observations) in dataset,
N_p : the number of samples in dataset belonging in positive class ($y = 1$),
N_n : the number of samples in dataset belonging in negative class ($y = 0$),

Table S1. Hyperparameters optimized for Extreme Gradient Boosting Classifier (XGBClassifier) predictive algorithm and the ranges of investigated values. The names of the parameters are identical to the names that appear in the corresponding Python library.

Predictive Algorithm	Hyperparameter	Investigated values
XGBClassifier Extreme Gradient Boosting Classifier	n_estimators	randint(10, 200)
	max_depth	randint(1, 12)
	learning_rate	uniform(0.01, 0.25)
	gamma	uniform(0.0, 10.0)
	reg_alpha	uniform(0.0, 10.0)
	reg_lambda	uniform(0.0, 10.0)

uniform() - randomly and uniformly select a float number from the range defined in parentheses; *randint()* - randomly and uniformly select an integer number from the range defined in parentheses

Table S2. SYNTAX Score Groups descriptive statistics.

		Syntax Score Groups						
		0 (α)		**1 to 22 (β)**		**>22 (γ)**		**P value*(pair)**
Sex	Female	103	37.20%	99	21.00%	53	25.20%	0.009 (α-γ)
	Male	174	62.80%	372	79.00%	157	74.80%	<0.001 (α-β)
	Total	277	100.00%	471	100.00%	210	100.00%	
Hypertension	No	132	47.70%	194	41.20%	72	34.30%	0.009 (α-γ)
	Yes	145	52.30%	277	58.80%	138	65.70%	
	Total	277	100.00%	471	100.00%	210	100.00%	
Diabetes Mellitus	No	206	74.40%	322	68.40%	114	54.30%	<0.001 (α-γ)
	Yes	71	25.60%	149	31.60%	96	45.70%	0.001 (β-γ)
	Total	277	100.00%	471	100.00%	210	100.00%	
Dyslipidaemia	No	180	65.00%	283	60.10%	131	62.40%	0.429
	Yes	97	35.00%	187	39.70%	79	37.60%	
	Total	277	100.00%	470	100.00%	210	100.00%	
Family history	No	235	84.80%	383	81.30%	170	81.00%	0.428
	Yes	42	15.20%	87	18.50%	40	19.00%	
	Total	277	100.00%	470	100.00%	210	100.00%	
Smoking	No	182	65.70%	231	49.00%	122	58.10%	<0.001 (α-β)
	Yes	95	34.30%	240	51.00%	88	41.90%	
	Total	277	100.00%	471	100.00%	210	100.00%	
Age (groups)	65<	150	54.20%	268	56.90%	86	41.00%	<0.001 (β-γ)
	65>	127	45.80%	201	42.70%	124	59.00%	0.01 (α-γ)
	Total	277	100.00%	469	100.00%	210	100.00%	
Previous Stroke	No	271	97.80%	456	96.80%	202	96.20%	0.669
	Yes	6	2.20%	15	3.20%	7	3.30%	
	Total	277	100.00%	471	100.00%	209	100.00%	
Peripheral vascular disease	No	269	97.10%	452	96.00%	193	91.90%	0.01 (α-γ)
	Yes	7	2.50%	19	4.00%	17	8.10%	
	Total	276	100.00%	471	100.00%	210	100.00%	
Aortic aneurysms	No	258	93.10%	466	98.90%	204	97.10%	<0.001 (α-β)
	Yes	19	6.90%	5	1.10%	5	2.40%	0.013 (α-γ)

	Total	277	100.00%	471	100.00%	209	100.00%	
Chronic pulmonary obstructive disease	No	258	93.10%	445	94.50%	201	95.70%	0.470
	Yes	19	6.90%	26	5.50%	9	4.30%	
	Total	277	100.00%	471	100.00%	210	100.00%	
Autoimmune disease	No	270	97.50%	467	99.20%	204	97.10%	0.099
	Yes	7	2.50%	4	0.80%	6	2.90%	
	Total	277	100.00%	471	100.00%	210	100.00%	
Atrial fibrillation	No	235	84.80%	430	91.30%	193	91.90%	0.033 (α-γ)
	Yes	42	15.20%	41	8.70%	17	8.10%	0.015 (α-β)
	Total	277	100.00%	471	100.00%	210	100.00%	
Known CAD	No	227	81.90%	384	81.50%	170	81.00%	0.01 (α-γ)
	Yes	5	1.80%	24	5.10%	20	9.50%	
	Total	232	100.00%	408	100.00%	190	100.00%	
Kidney GFR<55	No	246	88.80%	412	87.50%	160	76.20%	<0.001 (α-γ)
	Yes	25	9.00%	58	12.30%	44	21.00%	0.005 (β-γ)
	Total	271	100.00%	470	100.00%	204	100.00%	

*** Bonferroni corrected for multiple comparisons Kruskal Wallis test**

Table S3. Biochemical parameters per SYNTAX Score group

	SYNTAX Score						
	0 (α)		1 to 22 (β)		>22 (γ)		
	Mean(±SD)	±SD	Mean	±SD	Mean	±SD	P value*(pair)
BMI	28.47 (4.8)	4.8	28.61	4.62	28.4	4.23	0.853
Grace score	89(31)	31	107	36	119	36	<0.001 (α-β), <0.001 (α-γ), <0.001 (β-γ)
Total glucose	96.09(33.16)	33.16	95.65	36.17	84.61	36.59	0.002 (α-γ),0.001 (β-γ)
Creatinine	107.86	61.54	123.06	56.66	135.09	57.46	<0.001 (α-β), <0.001 (α-γ), 0.001 (β-γ)
Cholesterol	1.01	0.91	1.04	0.74	1.24	1.26	0.006 (α-β), <0.001 (α-γ)
Triglycerides	164.5	37.2	164.4	42.8	163.5	50.4	0.445
High density lipoprotein	129	117	160	142	156	141	<0.001 (α-β), 0.001 (α-γ)
Low density lipoprotein	47	14	41	12	41	12	<0.001 (α-β), <0.001 (α-γ)
High sensitivity Troponin T	93	31	94	37	92	43	0.33
Serum Glutamic-Oxaloacetic Transaminase	113.8	541.4	983.7	1967.2	862.1	1760	<0.001 (α-β), <0.001 (α-γ)
Serum Glutamic Pyruvic Transaminase	27.3	41.4	81.1	352.6	60.5	109	<0.001 (α-β), <0.001 (α-γ)
Lactate Dehydrogenase	191.1	2672.1	48	236	36.9	81.5	0.001 (α-β)
Creatine Phosphokinase	227	77	366	404	399	424	<0.001 (α-β), <0.001 (α-γ)
Low ventricular ejection fraction (%)	145	415	523	1227	472	986	<0.001 (α-β), <0.001 (α-γ)
Total glucose	0.54	0.1	0.5	0.11	0.48	0.12	<0.001 (α-β), <0.001 (α-γ)

* Bonferroni corrected for multiple comparisons Kruskal Wallis test

Table S4. CAD groups with proteins, ceramide, acylcarnitine and lipid levels

	CAD Groups																
	NSTEMI				**STEMI**				**Unstable Angina**				**Stable Angina**				**P value* (pair)**
N	**Median**	**↓95.0% CIs**	**↑95.0% CIs**		**N**	**Median**	**↓95.0% CIs**	**↑95.0% CIs**	**N**	**Median**	**↓95.0% CIs**	**↑95.0% CIs**	**N**	**Median**	**↓95.0% CIs**	**↑95.0% CIs**	
Proteins (N)																	
Galectin (ng/ml) (N=932)	164	8.41	7.6	9.4	216	10	9.1	10.9	136	9.36	8.87	10.9	416	9.82	9.3	10.4	0.099
NGAL(ng/ml)(119)	32	4.6	3	6.5	26	3.95	2	6.5	17	1.3	0.9	2.5	44	1.8	1.3	4.5	0.009 (δ-γ) 0.002 (γ-α)
Adiponectin (ng/ml)(N=216)	35	162	151.7	170	41	164	157	172	38	162.5	159	175	102	161	156	168	0.957
ApoB/ApoA-I(405)	66	0.86	0.77	1.15	112	0.93	0.85	1.01	64	0.82	0.66	0.97	163	0.75	0.68	0.86	0.11
Ceramides(N=915)																	
C16:0	163	0.546	0.513	0.571	214	0.629	0.574	0.654	134	0.52	0.48	0.54	404	0.487	0.471	0.511	0.01 (δ-α), <0.001 (δ-β),<0.001 (γ-α)
C18:0		0.214	0.196	0.237		0.243	0.225	0.272		0.192	0.186	0.216		0.176	0.164	0.19	<0.001 (δ-α), <0.001 (δ-β), 0.001 (γ-α)
C24:0		6.802	6.144	7.922		7.571	7.042	8.392		6.73	6.033	7.426		6.845	6.52	7.324	0.020 (γ-β), 0.029 (δ-β)
C24:1		3.137	2.889	3.66		3.566	3.317	3.866		2.859	2.614	3.3		2.962	2.872	3.146	0.001 (γ-β),<0.001 (δ-β)
Ratio C16:0/C24:0		0.081	0.076	0.087		0.073	0.07	0.081		0.073	0.069	0.078		0.07	0.067	0.074	0.002 (δ-α)
Ratio C18:0/C24:0		0.031	0.028	0.035		0.033	0.031	0.035		0.031	0.026	0.034		0.025	0.024	0.026	<0.001 (δ-α), <0.001 (δ-β), 0.01 (δ-γ)
Ratio C24:1/C24:0		0.457	0.434	0.511		0.456	0.428	0.48		0.454	0.425	0.49		0.436	0.419	0.459	0.329
Acyl L-carnitines (N=946)																	

C2	170	2906.5	2649.44	3154.25	219	2770.56	2539.3	3045.37	140	3147.27	2839.91	3452.4	417	2969.54	2846.84	3111.7	0.219
C3		168.35	151.99	182.39	219	173.55	157.15	191.74	140	181.15	167.93	196.96		176.8	169.84	185.38	0.824
C4		39.92	36.2	44.81		38.1	35.6	42.41		37.99	34.83	43.02		38.62	36.74	40.81	0.782
C5		24.79	23.46	28.8		29.08	26.36	30.73		25.13	22.86	27.7		25.72	24.95	27.5	0.026 (γ-β)
C6		27.46	25.83	31		27.58	25.65	29.1		30.69	27.77	33.83		29.98	28.87	31.46	0.329
C8		54.66	49	60.09		52.99	49.11	58.13		56.6	51.9	66.67		63.06	58.68	68.55	0.053
C10		89.88	78.25	105.42		86.53	79.36	94.45		91.5	83.49	110.42		106.09	96.74	116.37	0.019 (δ-β)
C12		26.54	23.7	30.2		27.96	25.11	29.83		29.17	24.86	31.54		29.88	28.26	31.39	0.377
C14		17.51	16.27	19.55		17.78	17.04	18.86		19.28	17.52	20.69		19.17	18.43	19.79	0.301
C16		58.38	55.03	63.64		58.29	55.82	60.89		62.9	60.82	66.52		63.21	60.85	65.63	0.012 (δ-β)
C18		17.35	16.09	18.35		18.63	17.76	19.54		18.63	17.49	19.29		19.01	18.45	19.59	0.137
C18:1		85.82	78.64	94.91		82.8	76.43	88.61		91.3	79.31	97.06		92.53	88.15	97.76	0.013 (δ-β)
C18:2		54.86	50.74	59.54		50.26	47.34	52.41		53.75	50	60.48		60.21	57.89	63.29	<0.001 (δ-β)
Fatty Acids (N=462)																	
C10:0	91	14.67	13.87	16.13	92	15.98	15.64	16.94	95	16.41	15.29	17.13	184	13.18	12.11	14.02	<0.001 (δ-β), <0.001 (γ-δ)
C12:0		28.73	27.81	31.14		29.44	28.54	30.65		29.62	28.43	31.41		23.16	20.82	26.11	0.003 (δ-β), <0.001 (γ-δ)
C14:0		49.89	41.67	59.51		47.99	42.57	60.06		63.19	55.12	71.9		50.39	43.27	58.8	0.064
C14:1		42.04	40.56	46.1		44.35	41.28	49.25		42.63	40.58	49.2		33.71	32.62	35.9	0.023 (δ-β), 0.042 (γ-δ)
C15:0		16.28	14.15	17.78		15.66	14.29	17.12		17.39	15.72	19.14		14.99	14.01	15.87	0.005 (δ-γ)
C16:0		1783.42	1516.81	2180.78		1806.5	1600.63	1949.54		1917.14	1644.89	2214.48		1270.19	1058.03	1424.22	<0.001 (δ-α), <0.001 (δ-β), <0.001 (δ-γ)
C16:1		94.15	79.93	118.22		99.42	83.32	113.49		106.56	92.24	123.12		68.97	57.24	80.95	<0.001 (δ-α), <0.001 (δ-β), <0.001 (δ-γ)

C17:0	21.01	17.67	24.46	20.52	17.25	22.4	22.7	18.68	24.4	13.13	11.68	15.85	<0.001 (δ-α), <0.001 (δ-β), <0.001 (δ-γ)
C17:1	117.66	116.37	119.77	116.88	115.79	118.2	117.93	117.12	122.37	98.18	80.71	112.47	<0.001 (δ-α), <0.001 (δ-β), <0.001 (δ-γ)
C18:0	479.75	418.05	581.89	515.56	411.87	602.13	549.42	458.23	632.56	373.24	300.2	431.84	0.003 (δ-α), 0.002 (δ-β), <0.001 (δ-γ)
cis_C18:1	1828.52	1687.32	2170.46	1765.11	1571.01	2024.97	1967.38	1721.87	2258.5	1413.07	1286.01	1575.49	<0.001 (δ-α), 0.002 (δ-β), <0.001 (δ-γ)
cis_C18:2	1852.94	1633.86	2049.21	1898.33	1699.97	2056.83	1903.79	1696.14	2232.47	1775.62	1600.89	1975.63	0.583
C18:3 n6	102.55	98.75	107.07	109.46	101.82	115.19	108.91	103.83	118.88	96.21	93.98	101.7	0.003 (δ-β), <0.001 (δ-γ)
C18:3 n3	90.57	85	97	94.93	89.27	99.13	96.43	90.85	99.01	83.57	81.96	84.79	0.004 (δ-α), <0.001 (δ-β), <0.001 (δ-γ)
C20:1n11	60.52	56.47	61.49	60.45	59.25	61.62	60.93	59.75	62.37	62.36	61.64	63.3	0.003 (δ-β)
C21:0	7.08	6.06	7.6	7.13	6.2	7.66	7.34	6.98	7.64	7	6.94	7.05	0.185
C20:2 cis	44.22	41.78	46.71	42.41	40.59	43.22	44.36	43.11	46.26	63.81	47.96	65.68	<0.001 (δ-β)
C22:0	73.71	63.53	74.97	74.51	73.15	75.63	74.07	72.4	75.38	48.56	47.58	51.34	<0.001 (δ-α), <0.001 (δ-β), <0.001 (δ-γ)

C20:3 w6		101.15	90.57	114.25		104.12	92.04	114.01		105.53	95.31	115.33	83.78	75.55	92.55	0.007 (δ-α), 0.005 (δ-β), 0.003 (δ-γ)
C20:4 w6		394.16	367.48	452.8		378.79	323.35	414.4		406.65	379.62	462.35	347.42	321.03	368.23	0.042 (δ-α), 0.012 (δ-γ)
C23:0		9.48	7.67	10.13		10.39	9.06	10.83		9.97	8.8	10.79	4.81	4.36	5.73	<0.001 (δ-α), <0.001 (δ-β), <0.001 (δ-γ)
C20:5 w3 cis		64.11	62.87	67.2		64.74	63.59	65.49		66.14	64.54	68.77	64.19	62.93	65.58	0.306
C24:0		62.57	60.94	67.55		67.07	62.41	68.66		65.08	61.19	68.42	43.39	40.58	46.08	<0.001 (δ-α), <0.001 (δ-β), <0.001 (δ-γ)
C24:1	90	67.34	65.38	68.55	88	66.47	64.43	67.51	94	67.34	65.36	69.46	181	63.44	62.49	64.39	<0.001 (δ-α), 0.002 (δ-β), <0.001 (δ-γ)
C22:6 w3 cis		95.63	91.47	100.97		100.87	92.5	106.34		102.09	95.85	110.54	93.92	90.43	98.55	0.169

* Bonferroni corrected for multiple comparisons Kruskal Wallis test

Table S5. Serum levels of proteins, ceramides and acyl-carnitines by CAD severity

	Syntax Score Groups												
	0 (α)				1 to 22 (β)				>22 (γ)				P value (pair) *
	N	Median	↓95.0% CIs	↑95.0% CIs	N	Median	↓95.0% CIs	↑95.0% CIs	N	Median	↓95.0% CIs	↑95.0% CIs	
Proteins (N)													
Galectin (ng/ml) (N=932)	270	10.3	9.3	10.9	457	9.1	8.7	9.77	205	10.1	9.55	11.27	0.065 (β-γ)
NGAL(ng/ml)(119)	22	1.75	0.7	5.3	57	2.4	1.8	4.2	40	3.2	1.9	6.5	0.29
Adiponectin (ng/ml)(N=216)	48	168	160	173	100	160	156	169	68	161.1	156	167	0.856
ApoB/ApoA-I(405)	134	0.69	0.63	0.8	194	0.88	0.82	0.96	77	0.86	0.76	1.05	0.005 (α-β)
Ceramides (N=915)													
C16:0	269	0.517	0.476	0.533	443	0.526	0.507	0.55	203	0.547	0.528	0.572	0.052 (α-γ)
C18:0	269	0.187	0.171	0.208	443	0.202	0.19	0.214	203	0.209	0.197	0.229	0.049 (α-β), 0.032 (α-γ)
C24:0	269	6.76	6.324	7.434	443	7.195	6.648	7.443	203	7.272	6.725	7.657	0.592
C24:1	269	2.906	2.837	3.197	443	3.18	3.069	3.352	203	3.223	3.06	3.506	0.052 (α-γ)
Ratio C16:0/C24:0	269	0.072	0.067	0.075	443	0.073	0.071	0.076	203	0.077	0.071	0.082	0.168
Ratio C18:0/C24:0	269	0.026	0.025	0.028	443	0.03	0.028	0.031	203	0.029	0.027	0.032	0.052 (α-β), 0.055 (α-γ)
Ratio C24:1/C24:0	269	0.434	0.414	0.452	443	0.459	0.435	0.475	203	0.454	0.43	0.48	0.19
Acyl L-carnitines (N=946)													
C2	273	3013.09	2848.26	3146.54	466	2841.43	2652.45	3047.79	207	2951.55	2798.57	3325.86	0.132
C3	273	171.49	162.86	179.56	466	175.68	167.86	184.94	207	186.56	170.45	209.04	0.084
C4	273	36.96	34.21	40.46	466	37.95	35.6	40.18	207	45.16	38.94	49.61	0.002 (α-γ), 0.005 (β-γ)
C5	273	25.25	23.99	26.36	466	26.41	24.95	28.63	207	27.82	25.34	30.79	0.024 (α-γ)
C6	273	29.81	28.07	33.04	466	28.89	27.63	30.08	207	28.88	27.1	31.34	0.889
C8	273	60.09	56.03	66.36	466	57.65	53.41	61.45	207	55.13	49.58	62.7	0.521
C10	273	99.63	90.03	109.52	466	94.48	86.47	101.15	207	92.32	80.54	104.81	0.43
C12	273	29.55	27.41	31.17	466	28.53	26.63	30.33	207	27.73	25.11	29.71	0.445
C14	273	19.24	18.12	20.36	466	18.54	17.59	19.27	207	18.21	17.06	19.69	0.229

C16	273	65.18	62.57	67.9	466	60.28	57.95	62.48	207	59.27	56.28	61.94	0.044 (α-β), 0.031(α-γ)
C18	273	19.11	18.27	20.08	466	18.39	17.7	19.03	207	18.18	17.5	19.08	0.166
C18:1	273	91.7	85.27	98.82	466	88.03	82.8	92.55	207	87.63	80.05	93.49	0.392
C18:2	273	60.48	56.37	64.61	466	53.83	51.35	56.62	207	53.28	49.37	57.57	0.019 (α-β), 0.012 (α-γ)
						Fatty Acids (N=462)							
C10:0	139	14.94	14.12	16.05	225	15.29	14.05	15.86	98	14.29	13.67	16.09	0.846
C12:0	139	28.38	26.4	29.56	225	28.7	27.96	29.47	98	26.69	21.75	28.09	0.107
C14:0	139	55.96	50.6	62.71	225	53.33	47	61.4	98	46.89	40.88	55.89	0.127
C14:1	139	40.84	34.73	43.44	225	41.14	40.35	42.06	98	40.76	31.05	48.63	0.589
C15:0	139	16.02	14.85	16.84	225	15.78	14.96	16.67	98	15.2	13.95	17.1	0.943
C16:0	139	1544.06	1362.65	1673.26	225	1643.83	1555.12	1828.46	98	1609.08	1372.24	1859.12	0.352
C16:1	139	85.08	76.05	105.34	225	92.22	82.63	98.1	98	78.78	73.05	94.68	0.37
C17:0	139	17.67	14.4	19.79	225	18.22	16.75	20.42	98	18.14	14.72	20.4	0.543
C17:1	139	115.78	114.35	116.85	225	115.56	114.8	116.39	98	117.46	116	118.72	0.036 (α-γ)
C18:0	139	446.6	396.67	505.74	225	467.38	412.25	529.82	98	446.83	347.43	522.85	0.859
cis_C18:1	139	1550.19	1388.97	1709.86	225	1814.8	1687.32	1893.56	98	1648.71	1470.54	1804.82	0.022 (α-β)
cis_C18:2	139	1915.14	1719.39	2020.69	225	1834.87	1678.13	1931.15	98	1859.13	1607.59	2101.85	0.874
C18:3 n6	139	103.83	100.34	110.49	225	103.52	100.49	107.56	98	101.51	98.75	106.37	0.636
C18:3 n3	139	90.05	84.82	94.49	225	89.27	85.42	91.73	98	89.38	85	96.64	0.64
C20:1n11	139	61.57	60.34	62.37	225	61.5	60.75	62.1	98	60.9	59.81	61.78	0.909
C21:0	139	7.03	6.97	7.16	225	6.98	6.89	7.08	98	7.23	7.08	7.49	0.116
C20:2 cis	139	46.07	43.97	49.28	225	44.36	43.14	46.91	98	45.8	43.24	50.49	0.597
C22:0	139	60.37	49.64	73.87	225	68.91	52.81	74.07	98	63.08	54.44	73.9	0.739
C20:3 w6	139	95.31	86.93	102.27	225	96.86	87.79	106.25	98	94.81	85.71	102.63	0.708
C20:4 w6	139	360.33	336.72	392.46	225	383.75	352.4	406.41	98	386.27	333.97	414.34	0.685
C23:0	139	7.85	5.57	9.59	225	8.14	6.49	9.63	98	7.83	5.97	9.86	0.695
C20:5 w3 cis	139	65.33	63.98	66.75	225	63.97	63.14	64.98	98	65.53	64.11	68.07	0.108

C24:0	139	61.29	46.08	64.93	225	61.54	59.94	62.56	98	59.63	48.34	67.55	0.76
C24:1	138	64.22	63.36	65.12	218	65.36	63.87	66.63	97	66.49	64.91	67.62	0.135
C22:6 w3 cis	139	96.86	91.97	100.2	225	94.29	91.86	100.69	98	100.57	94.83	105.82	0.282

* Bonferroni corrected for multiple comparisons Kruskal Wallis test