

Table 1 of the supplementary data. Characteristics of the potentially eligible participants included and not included in the analysis

	Not included	Included	P	Effect size	N
	n=2312	n=6468			
Age, y	53.6 ± 13.5	51.1 ± 12.3)	< .001	0.201	8780
Female sex	1242 (53.7)	3595 (55.6)	.128	0.016	8780
Body mass index, kg/m ²	27.5 ± 4.81	26.9 ± 4.38	< .001	0.134	8717
Smoking			< .001	0.047	8670
Never	1189 (52.3)	3573 (55.8)			
Current or former < 1 y	634 (27.9)	1493 (23.3)			
Former > 1 y	449 (19.8)	1332 (20.8)			
Diabetes mellitus	231 (9.99)	431 (6.66)	< .001	0.055	8780
Glycemia, mg/dL	96.0 [88.0;107]	94.0 [87.0;103]	< .001	0.177	8557
Hypertension	1030 (45.4)	2343 (37.0)	< .001	0.075	8597
Systolic blood pressure, mmHg	129 ± 20.6	125 ± 18.9	< .001	0.220	8753
Diastolic blood pressure, mmHg	78.8 ± 10.6	78.1 ± 10.2	.004	0.071	8742
Total cholesterol, mg/dL	218 ± 43.1	214 ± 41.7	< .001	0.099	8552
LDL cholesterol, mg/dL	144 ± 39.0)	140 ± 37.1	< .001	0.094	8322
HDL cholesterol, mg/dL	52.3 ± 14.3	52.5 ± 13.4	.523	-0.016	8527
Triglycerides, mg/dL	97.0 [70.0;135]	89.0 [66.0;123]	< .001	0.113	8535

LDL, low density lipoprotein; HDL, high density lipoprotein.

Continuous traits distribution is shown as mean ± standard deviation or median [interquartile range: Quartile 1; Quartile 3]. Categorical traits are shown as No. (%).

Effect size difference evaluation:

- Categorical: Cramer’s V little if any association (< 0.1), low (< 0.3), moderate (< 0.5), high (>0.5) [<https://www.acastat.com/statbook/chisqassoc.htm>]
- Quantitative: Cohen’s d negligible (< 0.2), small (< 0.5), medium (< 0.8), large (>0.8)

Table 2 of the supplementary data. Clinical and carotid stiffness indices characteristics in the group of participants without and with an ischemic heart disease event in the follow-up.

	No events n=6371	Ischemic heart disease n=97	P	N
Clinical characteristics				
Age, y	58.9 ± 12.0	66.8 ± 11.1	< .001	6468
Female sex	3559 (55.9)	36 (37.1)	< .001	6468
Body mass index, kg/m ²	27.2 ± 4.46	28.5 ± 4.58	.005	6462
Smoking			.094	6429
Never	3494 (55.2)	43 (44.3)		
Current or former < 1 y	1125 (17.8)	20 (20.6)		
Former > 1 y	1713 (27.1)	34 (35.1)		
Diabetes mellitus	566 (8.88)	22 (22.7)	< .001	6468
Glycemia, mg/dL	92.0 [85.8;101]	95.8 [87.7;107]	.002	6411
Hypertension	3058 (48.1)	73 (75.3)	< .001	6459
Systolic blood pressure, mmHg	129 ± 19.6	137 ± 19.9	< .001	6466
Diastolic blood pressure, mmHg	77.5 ± 10.1	79.9 ± 10.2	.025	6466
Total cholesterol, mg/dL	207 ± 35.9	211 ± 39.8	.328	6411
LDL cholesterol, mg/dL	134 ± 30.8	140 ± 35.5	.112	6343
HDL cholesterol, mg/dL	53.4 ± 12.0	49.8 ± 10.6	.001	6411
Triglycerides, mg/dL	86.0 [63.0;118]	102 [74.8;126]	.006	6412
Carotid stiffness indices				
Strain x 100	9.48 [7.96;11.1]	9.50 [7.29;11.2]	.441	6468
Stiffness parameter	5.65 [4.64;7.05]	6.34 [5.03;8.09]	.001	6467
Peterson elasticity coefficient x 0.1	7.14 [5.67;9.23]	8.37 [6.60;10.9]	< .001	6467
Compliance coefficient	0.82 [0.66;1.02]	0.79 [0.63;0.97]	.292	6468
Distensibility coefficient x 1000	30.0 [23.2;38.0]	26.1 [19.0;32.3]	< .001	6466
Pulse wave velocity	5.75 [5.10;6.57]	6.21 [5.53;7.16]	< .001	6467

HDL, high density lipoprotein; LDL, low density lipoprotein.

Continuous traits distribution is shown as mean ± standard deviation or median [interquartile range: Quartile 1; Quartile 3]. Categorical traits are shown as No. (%).

Table 3 of the supplementary data. Clinical and carotid stiffness indices characteristics in the group of participants without and with a cerebrovascular event in the follow-up.

	No event	Cerebrovascular disease	P	N
	n=6383	n=85		
Clinical characteristics				
Age, y	58.9 ± 12.0	70.5 ± 10.3	< .001	6468
Female sex	3554 (55.7)	41 (48.2)	.207	6468
Body mass index, kg/m ²	27.2 ± 4.46	28.3 ± 4.73	.032	6462
Smoking			.143	6429
Never	3483 (54.9)	54 (64.3)		
Current or former < 1 y	1136 (17.9)	9 (10.7)		
Former > 1 y	1726 (27.2)	21 (25.0)		
Diabetes mellitus	566 (8.87)	22 (25.9)	< .001	6468
Glycemia, mg/dL	92.0 [85.9;101]	96.6 [91.1;115]	< .001	6411
Hypertension	3064 (48.1)	67 (78.8)	< .001	6459
Systolic blood pressure, mmHg	129 ± 19.6	143 ± 20.1	< .001	6466
Diastolic blood pressure, mmHg	77.5 ± 10.1	79.6 ± 10.1	.059	6466
Total cholesterol, mmHg	207 ± 35.9	211 ± 39.1	.342	6411
LDL cholesterol, mmHg	134 ± 30.8	138 ± 32.1	.296	6343
HDL cholesterol, mmHg	53.4 ± 12.0	51.5 ± 12.3	.176	6411
Triglycerides, mmHg	86.0 [63.0;118]	104 [76.8;130]	.002	6412
Carotid stiffness indices				
Strain x 100	9.49 [7.97;11.1]	8.20 [6.60;10.7]	< .001	6468
Stiffness parameter	5.65 [4.63;7.04]	7.50 [5.70;9.68]	< .001	6467
Peterson elasticity coefficient x 0.1	7.13 [5.67;9.21]	10.2 [7.51;13.1]	< .001	6467
Compliance coefficient	0.82 [0.66;1.02]	0.66 [0.55;0.87]	< .001	6468
Distensibility coefficient x 1000	30.1 [23.2;38.0]	20.9 [16.2;29.8]	< .001	6466
Pulse wave velocity	5.74 [5.10;6.56]	6.88 [5.99;7.82]	< .001	6467

HDL, high density lipoprotein; LDL, low density lipoprotein.

Continuous traits distribution is shown as mean ± standard deviation or median [interquartile range: Quartile 1; Quartile 3]. Categorical traits are shown as No. (%).

Table 4 of the supplementary data. Clinical and carotid stiffness indices characteristics in the group of participants without and with a fatal event in the follow-up.

	No event	Mortality	P	N
	n=6157	n=311		
Clinical characteristics				
Age, y	58.4 ± 11.8	72.0 ± 10.5	< .001	6468
Female sex	3467 ± 56.3	128 ± 41.2	< .001	6468
Body mass index, kg/m ²	27.2 ± 4.45	27.8 ± 4.61	.020	6462
Smoking			< .001	6429
Never	3383 (55.3)	154 (49.5)		
Current or former < 1 y	1108 (18.1)	37 (11.9)		
Former > 1 y	1627 (26.6)	120 (38.6)		
Diabetes mellitus	503 (8.17)	85 (27.3)	< .001	6468
Glycemia, mg/dL	92.0 [85.7;101]	98.0 [90.0;115]	< .001	6411
Hypertension	2911 ± 47.3	220 ± 71.0	< .001	6459
Systolic blood pressure, mmHg	129 ± 19.5	139 ± 20.3	< .001	6466
Diastolic blood pressure, mmHg	77.6 ± 10.1	76.0 ± 10.5	.009	6466
Total cholesterol, mmHg	207 ± 35.7	202 ± 39.6	.015	6411
LDL cholesterol, mmHg	134 ± 30.7	129 ± 33.4	.011	6343
HDL cholesterol, mmHg	53.5 ± 12.0	51.4 ± 12.2	.004	6411
Triglycerides, mmHg	86.0 [63.0;118]	95.0 [72.0;124]	< .001	6412
Carotid stiffness indices				
Strain x 100	9.53 [8.01;11.1]	8.64 [7.06;10.7]	< .001	6468
Stiffness parameter	5.60 [4.61;6.97]	6.96 [5.75;8.59]	< .001	6467
Peterson elasticity coefficient x 0.1	7.07 [5.65;9.10]	9.22 [7.09;11.7]	< .001	6467
Compliance coefficient	0.82 [0.66;1.02]	0.71 [0.59;0.94]	< .001	6468
Distensibility coefficient x 1000	30.3 [23.5;38.2]	23.0 [18.2;30.7]	< .001	6466
Pulse wave velocity	5.72 [5.08;6.52]	6.55 [5.72;7.49]	< .001	6467

HDL, high density lipoprotein; LDL, low density lipoprotein.

Continuous traits distribution is shown as mean ± standard deviation or median [interquartile range: Quartile 1; Quartile 3]. Categorical traits are shown as No. (%).

Table 5 of the supplementary data. Multivariate adjusted association between each of the carotid stiffness indices and the outcomes of interest considering competing risk in women

	Strain HR (95 % CI) (per 0.01 units)	Stiffness HR (95%CI) (per 1 unit)	Peterson elasticity coefficient HR (95%CI) (per 10 units)	Compliance coefficient HR (95%CI) (per 1 unit)	Distensibility coefficient HR (95%CI) (per 0.001 units)	Pulse wave velocity HR (95%CI) (per 1 unit)
<i>PANEL A.- Linear association assumption</i>						
Ischemic heart disease	---	1.01 (0.89-1.13)	0.99 (0.89-1.11)	1.88 (0.42-8.28)	1.02 (0.97-1.07)	0.96 (0.69-1.33)
Cerebrovascular disease	0.99 (0.89-1.10)	1.04 (0.92-1.17)	1.02 (0.94-1.12)	1.25 (0.26-6.14)	1.00 (0.96-1.04)	1.11 (0.83-1.50)
Overall vascular disease	---	1.03 (0.94-1.11)	1.01 (0.95-1.08)	1.60 (0.55-4.64)	1.01 (0.98-1.04)	1.05 (0.84-1.31)
Overall mortality	1.01 (0.94-1.08)	1.00 (0.94-1.07)	1.01 (0.96-1.06)	1.21 (0.53-2.75)	1.01 (0.98-1.03)	1.02 (0.88-1.19)
<i>PANEL B.- Nonlinear association assumption</i>						
	Strain ≤ 0.09 HR (95% CI) (per 0.01 units)	Strain > 0.09 HR (95% CI) (per 0.01 units)				
Ischemic heart disease	0.97 (0.69-1.36)	1.13 (0.98-1.30)				
Overall vascular disease	0.91 (0.73-1.14)	1.07 (0.92-1.23)				

CI, confidence interval; HR, hazard ratio.

Adjusted for age, sex, body mass index, smoking, diabetes, systolic blood pressure, diastolic blood pressure, low density lipoprotein cholesterol, high density lipoprotein cholesterol, triglycerides. Competing risk: non-cardiovascular mortality as a competing event for ischemic heart disease and cerebrovascular disease, ischemic heart disease mortality as a competing event for cerebrovascular diseases, and cerebrovascular disease mortality as a competing event for ischemic heart disease.

Panel A: a linear association assumption is considered for all the indices.

Panel B: analysis of the association between strain and global vascular disease/ischemic heart disease was segmented according to the knot at which a change in the linear dose-response is observed (0.09), and strain is considered as a continuous variable in each of the defined segments, assuming a linear risk in each of the segments.

Table 6 of the supplementary data. Multivariate adjusted association between each of the carotid stiffness indices and the outcomes of interest considering competing risk in men

	Strain HR (95 % CI) (per 0.01 units)	Stiffness HR (95%CI) (per 1 unit)	Peterson elasticity coefficient HR (95%CI) (per 10 units)	Compliance coefficient HR (95%CI) (per 1 unit)	Distensibility coefficient HR (95%CI) (per 0.001 units)	Pulse wave velocity HR (95%CI) (per 1 unit)
<i>PANEL A.- Linear association assumption</i>						
Ischemic heart disease	---	0.98 (0.84-1.14)	1.00 (0.89-1.12)	1.89 (0.72-4.93)	1.02 (0.98-1.06)	0.95 (0.68-1.33)
Cerebrovascular disease	0.81 (0.71-0.93)	1.15 (1.07-1.24)	1.13 (1.06-1.21)	0.26 (0.06-1.03)	0.92 (0.88-0.97)	1.51 (1.25-1.82)
Overall vascular disease	---	1.07 (0.99-1.16)	1.08 (1.02-1.14)	0.99 (0.42-2.33)	0.99 (0.95-1.02)	1.20 (1.00-1.45)
Overall mortality	1.01 (0.95-1.08)	0.99 (0.93-1.06)	1.00 (0.95-1.05)	1.13 (0.64-2.01)	1.00 (0.98-1.02)	1.04 (0.90-1.21)
<i>PANEL B.- Nonlinear association assumption</i>						
	Strain ≤ 0.09 HR (95% CI) (per 0.01 units)	Strain > 0.09 HR (95% CI) (per 0.01 units)				
Ischemic heart disease	0.79 (0.57-1.11)	1.16 (1.02-1.33)				
Overall vascular disease	0.78 (0.64-0.95)	1.12 (1.00-1.26)				

CI, confidence interval; HR, hazard ratio.

Adjusted for age, sex, body mass index, smoking, diabetes, systolic blood pressure, diastolic blood pressure, low density lipoprotein cholesterol, high density lipoprotein cholesterol, triglycerides. Competing risk: noncardiovascular mortality as a competing event for ischemic heart disease and cerebrovascular disease, ischemic heart disease mortality as a competing event for cerebrovascular diseases, and cerebrovascular disease mortality as a competing event for ischemic heart disease.

Panel A: a linear association assumption is considered for all the indices.

Panel B: analysis of the association between strain and global vascular disease/ischemic heart disease was segmented according to the knot at which a change in the linear dose-response is observed (0.09), and strain is considered as a continuous variable in each of the defined segments, assuming a linear risk in each of the segments.

Figure 1 of the supplementary data. The 3 patterns shown in the dose-response association between carotid artery stiffness indices and the outcomes of interest.

