

SUPPLEMENTAL MATERIAL

Supplementary Table 1. Association between IMT progression and CMB, stratified by medication use and total cholesterol level.

Exposure	Stratification Variable (measured at exam 6)	CMB Location								
		Any CMB (n=101)			Lobar CMB (n=67)			Deep + Mixed CMB (n=34)		
		OR (95% CI)	P-value	P-value for interaction	OR (95% CI)	P-value	P-value for interaction	OR (95% CI)	P-value	P-value for interaction
Change in CCA IMT (per SD* increment)	Antihypertensive treatment									
	No	0.78 (0.53-1.15)	0.22		0.93 (0.62-1.39)	0.72		0.54 (0.27-1.09)	0.08	
	Yes	0.89 (0.62-1.29)	0.55	0.68	1.04 (0.81-1.32)	0.78	0.68	0.38 (0.17-0.87)	0.02	0.53
	Statin use									
	No	0.98 (0.78-1.23)	0.88		1.06 (0.88-1.28)	0.54		0.60 (0.31-1.14)	0.12	
	Yes	0.43 (0.20-0.92)	0.03	0.06	0.77 (0.35-1.68)	0.51	0.45	0.24 (0.08-0.73)	0.01	0.27
	Antithrombotic therapy use									
	No	0.87 (0.63-1.20)	0.39		1.05 (0.77-1.44)	0.75		0.43 (0.21-0.91)	0.03	
	Yes	0.89 (0.57-1.39)	0.61	0.82	1.04 (0.79-1.36)	0.79	0.99	0.46 (0.21-1.03)	0.06	0.84
	Total cholesterol ≥10 th percentile									
No	1.06 (0.55-2.04)	0.87		1.28 (0.61-2.69)	0.51		**	**		
Yes	0.86 (0.64-1.14)	0.29	0.67	1.03 (0.83-1.27)	0.81	0.93	0.40 (0.23-0.72)	0.002	0.20	
Change in ICA IMT (per SD* increment)	Antihypertensive treatment									
	No	1.04 (0.81-1.34)	0.74		1.03 (0.76-1.38)	0.87		1.06 (0.70-1.61)	0.80	
	Yes	1.28 (0.91-1.80)	0.16	0.37	1.22 (0.80-1.87)	0.35	0.51	1.37 (0.83-2.27)	0.22	0.47
	Statin use									
	No	1.10 (0.88-1.38)	0.41		1.14 (0.87-1.48)	0.34		1.01 (0.68-1.50)	0.97	
	Yes	1.22 (0.77-1.92)	0.39	0.58	0.98 (0.65-1.49)	0.93	0.65	1.99 (0.95-4.16)	0.07	0.09
	Antithrombotic therapy use									
	No	1.14 (0.87-1.48)	0.34		1.11 (0.80-1.53)	0.52		1.22 (0.77-1.91)	0.40	
	Yes	1.12 (0.82-1.52)	0.47	0.98	1.08 (0.75-1.55)	0.68	0.96	1.15 (0.73-1.80)	0.55	0.78
	Total cholesterol ≥10 th percentile									
No	1.28 (0.62-2.65)	0.51		1.30 (0.53-3.17)	0.56		**	**		
Yes	1.13 (0.92-1.39)	0.26	0.92	1.10 (0.86-1.41)	0.44	0.86	1.17 (0.84-1.62)	0.36	0.71	

All models are adjusted for age, sex, and years between exam 8 and MRI.

*A 1 standard deviation (SD) increment is 0.010 for CCA IMT and 0.087 for ICA IMT.

**Insufficient sample size to calculate stratum-specific effect estimates.—

ICA= internal carotid artery, CCA= common carotid artery, IMT= intima media thickness, CMB= cerebral microbleeds, OR= odds ratio, CI= confidence interval.

Supplementary table 2. Clinical characteristics among participants with carotid IMT progression by hypertension treatment (N=1238)

	No antihypertensive treatment (N=976)	Antihypertensive treatment (N=262)	p-value
<i>Clinical Characteristics</i>			
Women, n (%)	546 (55.9)	114 (43.5)	0.0003
Age at Exam 6, yrs, mean [SD]	55.6 (8.6)	61.3 (8.0)	<0.0001
Age at Exam 8, yrs mean [SD]	65.1 (8.6)	70.6 (8.0)	<0.0001
Age at MRI testing, yrs, mean [SD]	65.7 (8.5)	71.2 (7.9)	<0.0001
<i>Exam 6 Covariates</i>			
Systolic blood pressure, mm Hg, mean [SD]	122 (17)	136 (18)	<0.0001
Diastolic blood pressure, mm Hg, mean [SD]	74 (9)	79 (10)	<0.0001
Pulse Pressure (SBP-DBP), mean [SD]	48 (13)	58 (16)	<0.0001
Diabetes mellitus, n (%)	42 (4.3)	50 (19.3)	<0.0001
Current smokers, n (%)	137 (14.0)	23 (8.8)	0.02
Prevalent cardiovascular disease, n (%)	30 (3.1)	46 (17.6)	<0.0001
Total cholesterol level, mg/dL, mean [SD]	205 (37)	199 (34)	0.02
Lipid lowering therapy use, n (%)	62 (6.4)	69 (26.4)	<0.0001
Statin use, n (%)	51 (5.2)	56 (21.5)	<0.0001
Antithrombotic use, n (%)	205 (21.0)	121 (46.2)	<0.0001
APOE ε4 (any)	200 (20.7)	63 (24.5)	0.19

Note: 5 participants are missing information on hypertension treatment.

SBP= Systolic Blood Pressure, DBP= Diastolic Blood Pressure, IMT= intima media thickness, SD= standard deviation.

Supplementary Table 3. Association between CCA IMT progression and CMB, stratified by vascular risk factors.

Exposure	Stratification Variable (measured at exam 6)	CMB Location								
		Any CMB (n=101)			Lobar CMB (n=67)			Deep + Mixed CMB (n=34)		
		OR (95% CI)	P-value	P-value for interaction	OR (95% CI)	P-value	P-value for interaction	OR (95% CI)	P-value	P-value for interaction
Change in CCA IMT (per SD* increment)	Diabetes									
	No	0.93 (0.71-1.21)	0.58		1.03 (0.83-1.28)	0.79		0.57 (0.31-1.06)	0.08	
	Yes	0.73 (0.39-1.36)	0.32	0.33	1.08 (0.55-2.09)	0.83	0.97	0.34 (0.12-0.99)	0.047	0.36
	Smoking									
	No	0.96 (0.73-1.26)	0.75		1.14 (0.88-1.49)	0.32		0.48 (0.27-0.86)	0.01	
	Yes	0.34 (0.09-1.20)	0.09	0.16	0.53 (0.15-1.86)	0.32	0.47	0.17 (0.02-1.54)	0.11	0.24
	Hypertension									
	No	0.89 (0.58-1.37)	0.60		1.05 (0.66-1.66)	0.84		0.57 (0.23-1.38)	0.21	
	Yes	0.78 (0.52-1.16)	0.21	0.68	0.98 (0.72-1.33)	0.90	0.95	0.38 (0.19-0.79)	0.01	0.49
	Blood pressure ≥140/90 mm Hg									
	No	0.81 (0.57-1.15)	0.24		1.09 (0.77-1.55)	0.62		0.34 (0.17-0.67)	0.002	
	Yes	0.94 (0.66-1.34)	0.74	0.59	1.01 (0.75-1.36)	0.97	0.79	0.66 (0.25-1.69)	0.38	0.40
	Age ≥65 years									
	No	0.82 (0.54-1.24)	0.33		1.00 (0.74-1.33)	0.97		0.37 (0.17-0.80)	0.01	
	Yes	0.90 (0.64-1.28)	0.57	0.94	1.10 (0.77-1.56)	0.61	0.86	0.48 (0.22-1.01)	0.05	0.53
	Male sex									
No	0.75 (0.47-1.18)	0.21		1.09 (0.69-1.71)	0.71		0.31 (0.14-0.66)	0.002		
Yes	0.93 (0.70-1.25)	0.63	0.46	1.01 (0.78-1.30)	0.95	0.69	0.63 (0.31-1.30)	0.21	0.17	

All models are adjusted for age, sex, and years between exam 8 and MRI.

*A 1 standard deviation (SD) increment is 0.010 for CCA IMT.

CCA= common carotid artery, IMT= intima media thickness, CMB= cerebral microbleeds, OR= odds ratio, CI= confidence interval.

Supplementary Table 4. Association between CCA IMT* progression and CMB, stratified by antihypertensive medication use and blood pressure level.

Anti-hypertensive treatment**	Blood pressure level (mm Hg)**	N	CMB Location								
			Any CMB (n=101)			Lobar CMB (n=67)			Deep + Mixed CMB (n=34)		
			OR (95% CI)	P-value	P-value for interaction***	OR (95% CI)	P-value	P-value for interaction***	OR (95% CI)	P-value	P-value for interaction***
No	<140/90	821	0.89 (0.58-1.37)	0.60		1.05 (0.66-1.66)	0.84		0.57 (0.23-1.38)	0.21	
	≥140/90	143	0.27 (0.07-1.02)	0.05		†	†		0.41 (0.08-2.01)	0.27	
Yes	<140/90	150	0.48 (0.23-0.99)	0.046		0.94 (0.42-2.09)	0.87		0.17 (0.06-0.54)	0.003	
	≥140/90	112	1.05 (0.82-1.34)	0.70	0.09	1.06 (0.83-1.35)	0.66	0.73	0.98 (0.31-3.09)	0.97	0.10

All models are adjusted for age, sex, and years between exam 8 and MRI.

*A 1 standard deviation (SD) increment is 0.010 for CCA IMT.

**Measured at exam 6 (baseline).

***Likelihood ratio test (df=4) for the three-way interaction between antihypertensive treatment, blood pressure category, and change in CCA IMT.

† Insufficient sample size to calculate stratum specific estimates.

CCA= common carotid artery, IMT= intima media thickness, CMB= cerebral microbleeds, OR= odds ratio, CI= confidence interval.

Supplementary Table 5. Association between CCA IMT progression and CMB, stratified by antihypertensive medication type.

Exposure	Anti-hypertensive treatment type**	N	CMB Location					
			Any CMB		Lobar CMB		Deep + Mixed CMB	
			OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Change in CCA IMT (per SD* increment)	Diuretic	60	1.30 (0.86-1.97)	0.22	1.61 (0.97-2.67)	0.07	0.93 (0.41-2.12)	0.86
	Calcium channel blocker	75	0.82 (0.35-1.92)	0.65	0.61 (0.17-2.22)	0.45	1.61 (0.50-5.18)	0.43
	ACE inhibitor or ARB	115	0.96 (0.59-1.58)	0.88	1.44 (0.91-2.30)	0.12	0.12 (0.03-0.56)	0.007
	Beta blocker	81	1.05 (0.49-2.25)	0.91	1.00 (0.31-3.24)	0.99	1.10 (0.42-2.84)	0.85

All models are adjusted for age, sex, and years between exam 8 and MRI.

*A 1 standard deviation (SD) increment is 0.010 for CCA IMT.

**Measured at exam 6 (baseline).

CCA= common carotid artery, IMT= intima media thickness, CMB= cerebral microbleeds, ACE= angiotensin converting enzyme, ARB= angiotensin receptor blocker, OR= odds ratio, CI= confidence interval.