Supplementary Material

SM1.1. Study Population and Distribution of Patients

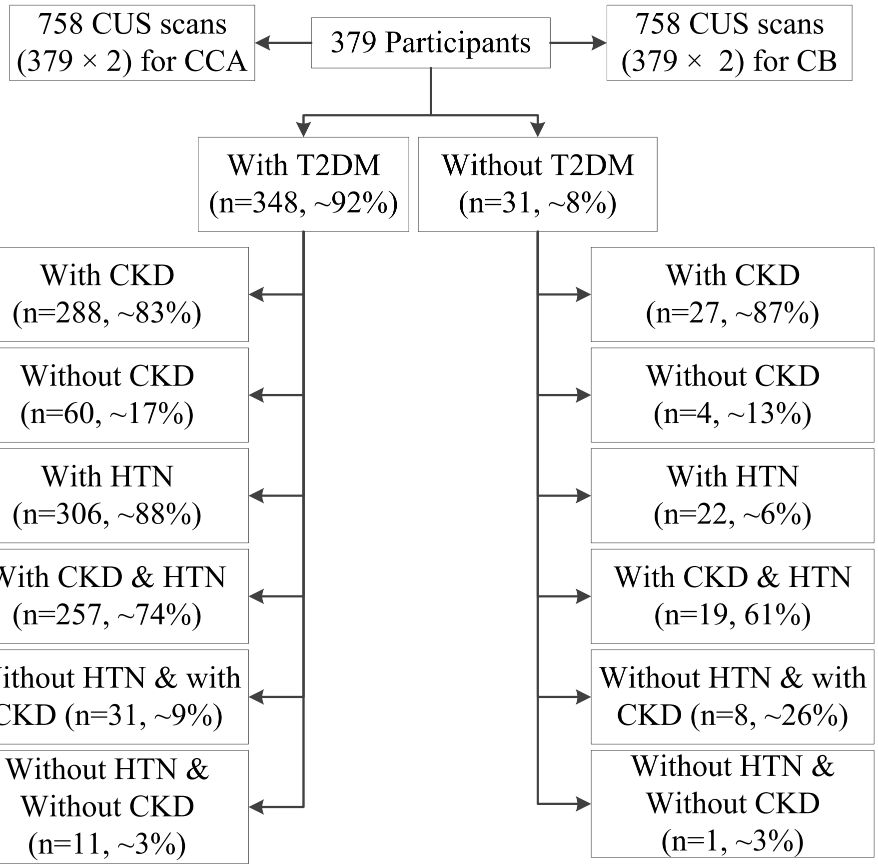

Figure SM1. Study population flow diagram. CUS: carotid ultrasound, CCA: common carotid artery, CB: carotid bulb, T2DM: type 2 diabetes mellitus, CKD: chronic kidney disease, and HTN: hypertension.

SM1.2. Power Analysis and Sample Size

The current study includes 1516 carotid ultrasound (CUS) scans from the 379 participants. As discussed in the section "Study Population and Selection Criteria," 4 scans were collected from each participant corresponding to left common carotid artery (LCCA), right common carotid artery (RCCA), left carotid bulb (LCB) and right carotid bulb (RCB). Note that although the carotid arteries (both left and right) have similar function (providing oxygenated blood to the brain), they work independently along 2 diverse pathways with the left carotid artery originating directly from the aortic arch and right carotid artery from the innominate artery.[1-4] Also, since atherosclerosis is a multifocal disease, plaque deposition within the left and right carotid arteries is at different locations and with difference in area or volume.[5,6] Thus, the current study uses a standardized protocol for data collection in which multiple samples were collected from different locations of the carotid arteries of the same participant. Thus, the adequate sample size for this study was 1516 (758 from common carotid artery or CCA and 758 from carotid bulb or CB). A power analysis was performed to validate this sufficient sample size. The motivation for performing power analysis was to identify the smallest sample size required to conduct the current study. In our study, the population refers to the sample size of 1516 scans derived from the Asian-Indian cohort. Considering the confidence level of 95%, a margin of error (MoE) of 5%, and a data proportion ($\hat{p}$) of 0.5, desired sample size (n) can be computed using $n = \left[(z^*)^2 \times \left(\frac{\hat{p}(1-\hat{p})}{\mathrm{MoE}^2}\right)\right]$.[7] Note that z^* is the z-score obtained from the normal distribution. The value of z^* is equal to 1.96 for a 95% confidence level (CI). Thus, the resultant sample size with a 95% CI and MoE of 5% was ~384. Thus recruited sample size (n=1516) was far greater than the desired sample size of 384. Note that as per our assumption, due to the combination of the geometry of carotid artery and atherosclerotic disease formation[5,6], we consider the ultrasound scans for LCCA, RCCA, LCB, and RCB to be independent.

SM1.3. Distribution of plaque area (PA) in 4 types of carotid artery segments

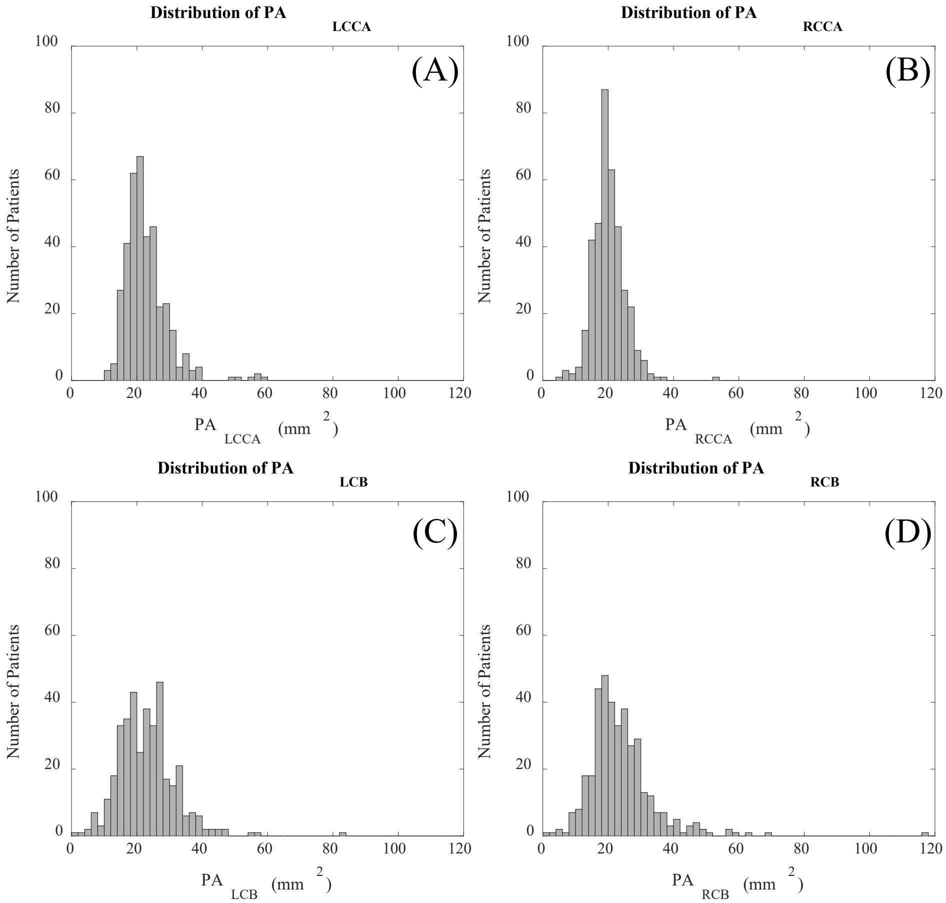

Figure SM2. Distribution of plaque area in 4 types of carotid artery segments: (A) LCCA, (B) RCCA, (C) LCB, (D) RCB.

PA: plaque area, LCCA: left common carotid artery, RCCA: right common carotid artery, LCB: left carotid bulb, RCB: right carotid bulb, PA_{LCCA}: plaque area from left common carotid artery, PA_{RCCA}: plaque area from right common carotid artery, PA_{LCB}: plaque area from left carotid bulb, PA_{RCB}: plaque area from right carotid bulb.

SM1.4. Ranking of 10-year risk cardiovascular disease risk calculators

Figure 8 shows the receiver operating characteristics (ROC) curves for 14 types of cardiovascular disease (CVD) risk calculators that include 2 integrated risk calculators and 12 types of conventional cardiovascular risk calculators. The area-under-the-curve (AUC) for two integrated risk calculators, such as AECRS2.0 (CB) and AECRS2.0 (CCA) (AUC=0.93 and AUC=0.83), is higher compared with the mean AUC of the 12 types of conventional cardiovascular risk calculators (AUC=0.62, p=0.06). The reason for the higher AUC is the inclusion of both conventional risk factors and the carotid ultrasound image-based phenotypes (CUSIP) that better explains the morphological variations in the plaque. Among the 12 types of conventional risk calculators, QRISK3 was ranked in the first place (AUC=0.77, p<0.0001), followed by the atherosclerosis CVD (ASCVD) calculator developed by American College of Cardiology/American Heart Association (ACC/AHA). The QRISK3 calculator was derived using a longitudinal follow-up study of 15 years on a diverse ethnicity cohort. Derivation of the model of QRISK3 included a cohort of Indian ethnicity, and this can be one of the reasons for the higher AUC compared with other risk calculators. Furthermore, QRISK3 is the only calculator that included the status of chronic kidney disease (CKD) while predicting the CVD risk. Out of 379 participants, ~83% (n=315) patients were having CKD (eGFR <90 ml/min/1.73m^2). This can be another reason for its higher AUC compared with other risk calculators. All the 12 types of conventional CVD risk calculators were derived for populations with different ethnicity, baseline characteristics, and the risk profile. Thus, there may be a possibility of variations in the results when these calculators are used on a single database, for they are not developed. Thus, the results can be validated by performing extensive validation using a common database. A short description is provided under the limitation section of the main manuscript.

SM1.5. Comparing atherosclerosis aggregation factors of CCA and CB

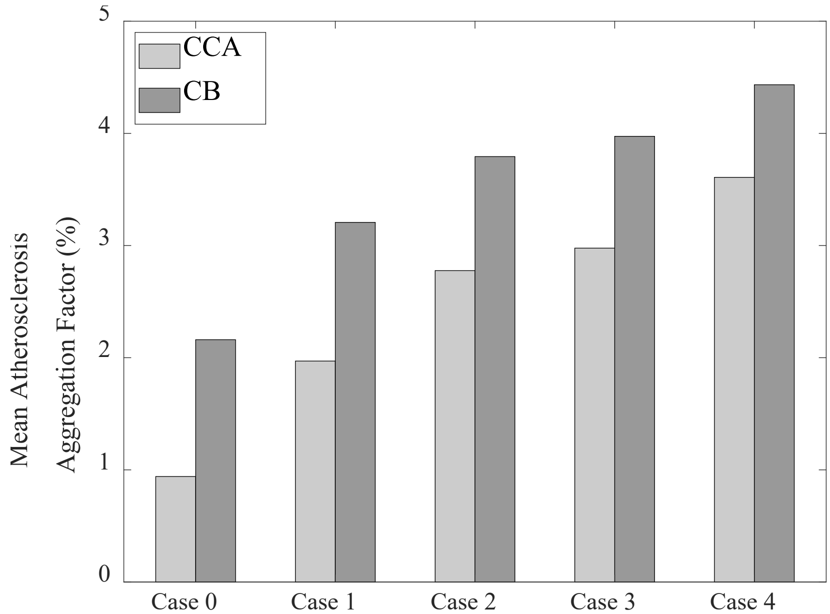

Figure SM3. Atherosclerosis aggregation factor in 5 different cases with a reference age of 20 years. Case 0: only 5 CUSIP, Case 1: 5 CUSIP and 10 types of conventional risk factors, Case 2: 5 CUSIP, 10 types of conventional risk factors, and eGFR, and, Case 3: 5 CUSIP, 10 types of conventional risk factors and ESR, and Case 4: 5 CUSIP, 10 types of conventional risk factors, ESR and eGFR.

CCA: common carotid artery, CB: carotid bulb, CUSIP: carotid ultrasound image-based phenotypes, eGFR: estimated glomerular filtration rate, ESR: erythrocyte sedimentation rate.

SM1.6. Results in tabulated format.

Table A1. Mean CVD/stroke risk in overall CCA *vs* CB.

Risk in case 0 (%)		Risk in case 1 (%)		Risk in case 2 (%)		Risk in case 3 (%)		Risk in case 4 (%)	
CCA	CB	CCA	CB	CCA	CB	CCA	CB	CCA	CB
15.43±9.62	25.10±14.72	23.60±11.09	33.41±13.49	29.99±12.53	38.06±13.52	31.59±11.23	39.51±12.18	36.60±12.37	43.16±12.36
CVD: cardiovascular disease, CCA: common carotid artery, CB: carotid bulb.									

Table A2. Mean CVD/stroke risk in CCA *vs* CB in patients with and without T2DM.

Type of Cohort	Risk in case 0 (%)		Risk in case 1 (%)		Risk in case 2 (%)		Risk in case 3 (%)		Risk in case 4 (%)	
	CCA	CB	CCA	CB	CCA	CB	CCA	CB	CCA	CB
Without T2DM	13.74±7.11	22.85±13.87	20.91±9.57	30.86±12.87	26.13±10.88	35.08±12.72	27.82±10.29	36.66±11.23	32.42±11.27	40.12±10.97
With T2DM	15.58±9.80	25.30±14.79	23.84±11.19	33.63±13.53	30.34±12.62	38.32±13.56	31.93±11.26	39.76±12.24	36.97±12.41	43.43±12.45
CVD: cardiovascular disease, CCA: common carotid artery, CB: carotid bulb, T2DM: type 2 diabetes mellitus.										

Table A3. Mean CVD/stroke risk in CCA *vs* CB in patients without CKD.

Type of Cohort	Risk in case 0 (%)		Risk in case 1 (%)		Risk in case 2 (%)		Risk in case 3 (%)		Risk in case 4 (%)	
	CCA	CB	CCA	CB	CCA	CB	CCA	CB	CCA	CB
Without CKD	14.65±9.11	23.80±13.86	22.57±10.80	32.14±12.98	26.38±10.87	35.04±12.55	29.97±10.88	37.98±11.70	33.05±10.87	40.32±11.30
With CKD	18.21±10.85	29.73±16.68	27.26±11.39	37.92±14.35	42.89±9.13	48.83±11.18	37.35±10.56	44.98±12.31	49.24±8.56	53.27±10.59
CVD: cardiovascular disease, CCA: common carotid artery, CB: carotid bulb, CKD: chronic kidney disease.										

Table A4. Mean CVD/stroke risk in CCA *vs* CB in patients with T2DM and CKD.

Risk in case 0 (%)		Risk in case 1 (%)		Risk in case 2 (%)		Risk in case 3 (%)		Risk in Case 4 (%)	
CCA	CB	CCA	CB	CCA	CB	CCA	CB	CCA	CB
16.14±10.02	26.37±15.02	24.73±11.11	34.70±13.54	32.41±12.00	40.21±13.09	33.15±10.83	40.90±12.18	39.10±11.52	45.21±12.00

CVD: cardiovascular disease, CCA: common carotid artery, CB: carotid bulb, T2DM: type 2 diabetes mellitus, CKD: chronic kidney disease.

Table A5. Mean CVD/stroke risk in LCCA *vs* RCCA.

Risk in Case 0 (%)		Risk in Case 1 (%)		Risk in Case 2 (%)		Risk in Case 3 (%)		Risk in Case 4 (%)	
LCCA	RCCA	LCCA	RCCA	LCCA	RCCA	LCCA	RCCA	LCCA	RCCA
17.41±11.25	13.45±7.14	25.76±12.17	21.44±9.42	31.93±12.89	28.05±11.86	33.47±11.77	29.71±10.33	38.28±12.56	34.91±11.96
CVD: cardiovascular disease, LCCA: left common carotid artery, RCCA: right common carotid artery.									

Table A6. Mean CVD/stroke risk in LCB *vs* RCB.

Risk in Case 0 (%)		Risk in Case 1 (%)		Risk in Case 2 (%)		Risk in Case 3 (%)		Risk in Case 4 (%)	
LCB	RCB	LCB	RCB	LCB	RCB	LCB	RCB	LCB	RCB
24.89±14.06	25.32±15.37	33.06±13.04	33.75±13.94	37.77±12.85	38.35±14.17	39.04±11.73	39.98±12.62	42.77±11.63	43.54±13.06
CVD: cardiovascular disease, LCB: left carotid bulb, RCB: right carotid bulb.									

Table A7. Atherosclerotic aggregation factor.

Healthy Age (years)	Risk in Case 0 (%)			Risk in Case 1 (%)			Risk in Case 2 (%)			Risk in Case 3 (%)			Risk in Case 4 (%)		
	CCA	CB	Improve.	CCA	CB	Improve.	CCA	CB	Improve.	CCA	CB	Improve.	CCA	CB	Improve.
20	0.94	2.16	130	1.97	3.21	63	2.78	3.79	37	2.98	3.97	33	3.61	4.43	23
25	0.83	1.97	139	1.80	2.96	65	2.56	3.51	37	2.74	3.68	34	3.34	4.11	23
30	0.48	1.41	196	1.26	2.20	75	1.87	2.65	41	2.03	2.79	37	2.51	3.13	25
35	0.58	1.57	172	1.41	2.42	71	2.07	2.89	39	2.23	3.03	36	2.74	3.40	24
40	0.50	1.44	187	1.30	2.24	72	1.94	2.70	39	2.08	2.83	36	2.58	3.19	24
CVD: cardiovascular disease, CCA: common carotid artery, CB: carotid bulb, Improve: Improvement.															

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