

SUPPLEMENTAL MATERIAL

Data S1. Supplemental Methods.

Data Screening and Extraction

Two raters independently screened titles/abstracts and full-text with discrepancies resolved by a third rater and by consensus, respectively. Inclusion and exclusion criteria for review of imaging modalities/techniques and imaging biomarker criteria for complex aortic arch plaque in cryptogenic stroke patients are listed below in Supplemental Table 2. Detailed inclusion and exclusion criteria for calculation of prevalence of complex aortic plaque in cryptogenic stroke patients are listed in Supplemental Table 3.

Two independent reviewers extracted data with discrepancies resolved by consensus. For studies that included both cryptogenic and non-cryptogenic stroke patients, only cryptogenic stroke patients were included for analysis. In addition, for derivation of complex aortic arch plaque prevalence, only acute/subacute infarct/data were included for analysis.

List of variables extracted from each study included the following:

- Study design details: prospective/retrospective design, study type, study setting, single/multi-site, dates of recruitment, funding source
- Imaging acquisition methods: Primary imaging modality, Time of imaging performed relative to stroke, time of imaging performed to confirm stroke, modality equipment details, reported technique of image acquisition, who acquired the image, who interpreted the image, segment of aorta imaged, how the segments of aorta were defined
- Plaque features: definition of plaque, definition of complex plaque, plaque features recorded, plaque grading system
- Patient cohort details: exclusion criteria (excluded cervical stenosis, cervical occlusion, intracranial stenosis >50%, carotid dissection, vasculitis, coagulopathy, migraines, prior stroke or transient ischemic attack, aortic dissection), reporting of patients as “cryptogenic” stroke or “undetermined source”, exclusion of cardiac findings such as atrial fibrillation, sick sinus syndrome, myocardial infarction, intracardiac thrombus, endocarditis, left ventricular aneurysm, dilated cardiomyopathy, arch tumor, prosthetic valve, mitral stenosis, spontaneous echo contrast, lack of acoustic window.
- Stroke type: whether the stroke was confirmed by imaging (CT or MRI) or by clinical findings, inclusion/exclusion of patients with transient ischemic attack, stroke topography (embolic, anterior circulation, posterior circulation, exclusion of lacunar infarcts), stroke timing definition
- Subject details: total number of cryptogenic stroke cases and by gender and age of patients. If available, above for control population.
- Study results: number of plaque by aortic segment, number of patients with complex aortic plaque, any other sources of cardiogenic embolic sources identified

Table S1: Search Strategy

The exact search strategies are provided below for open access.

<p>PubMed Search Strategy Code:</p> <p>((echocardiogram[MeSH]) OR (echocardiogram[All Fields]) OR (trans thoracic echocardiography [MeSH]) OR ("trans thoracic"[All Fields] AND "echocardiography"[All Fields]) OR ("TTE"[All Fields]) OR (TTE [MeSH]) OR (CT [MeSH]) OR ("computed tomography" [MeSH]) OR ("computed"[All Fields] AND "tomography"[All Fields]) OR ("computed tomography"[All Fields]) OR (CT [All Fields]) OR (magnetic resonance imaging[MeSH Terms]) OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields] OR "mri"[All Fields] OR "magnetic resonance imaging"[All Fields]) OR (transesophageal echocardiography [MeSH]) OR ("transesophageal"[All Fields] AND "echocardiography"[All Fields]) OR ("TEE"[All Fields]) OR (TEE [MeSH]) OR (computed tomography angiography [MeSH]) OR ("computed"[All Fields] AND "tomography"[All Fields] AND "angiography"[All Fields]) OR "computed tomography angiography"[All Fields] OR "CTA"[All Fields]) OR ("blood vessels"[MeSH Terms]) OR ("blood"[All Fields] AND "vessels"[All Fields]) OR "blood vessels"[All Fields] OR ("vessel"[All Fields] AND "wall"[All Fields] AND "imaging"[All Fields] AND "blood vessels"[MeSH Terms]) OR (spectral CT [All Fields]) OR ("spectral"[All Fields] AND "computed"[All Fields] AND "tomography"[All Fields]) OR "Spectral Computed Tomography"[All Fields]) OR (vessel[All Fields] AND wall[All Fields] AND MR[All Fields] AND imaging[All Fields]) OR (high[All Fields] AND resolution[All Fields] AND ("blood vessels"[MeSH Terms]) OR ("blood"[All Fields] AND "vessels"[All Fields]) OR ("blood vessels"[All Fields]) OR ("vessel"[All Fields] AND wall[All Fields] AND MR[All Fields] AND imaging[All Fields])) AND ((infarction[MeSH Terms]) OR "infarction"[All Fields] OR "infarct"[All Fields]) OR ("cerebral arterial diseases"[MeSH Terms]) OR ("cerebral"[All Fields] AND "arterial"[All Fields] AND "diseases"[All Fields]) OR "cerebral arterial diseases"[All Fields] OR ("cerebral"[All Fields] AND "arterial"[All Fields] AND "disease"[All Fields]) OR "cerebral arterial disease"[All Fields] OR "cerebral artery disease"[All Fields]) OR (arterial occlusive diseases[MeSH Terms]) OR ("arterial"[All Fields] AND "occlusive"[All Fields] AND "diseases"[All Fields]) OR "arterial occlusive diseases"[All Fields]) OR Stroke[MeSH] OR (brain ischaemia[All Fields] OR "brain ischemia"[MeSH Terms]) OR ("brain"[All Fields] AND "ischemia"[All Fields]) OR "brain ischemia"[All Fields]) OR (embolism[MeSH Terms]) OR "embolism"[All Fields]) OR Stroke/Etiology[MeSH] OR Brain Ischemia/Etiology[MeSH] OR Stroke/Diagnosis[MeSH] OR (transient ischaemic attack[All Fields] OR "ischemic attack, transient"[MeSH Terms]) OR ("ischemic"[All Fields] AND "attack"[All Fields] AND "transient"[All Fields]) OR "transient ischemic attack"[All Fields] OR ("transient"[All Fields] AND "ischemic"[All Fields] AND "attack"[All Fields]) OR TIA [All Fields]) OR Brain Ischemia/Diagnosis [MeSH] OR ("Cryptogenic"[All Fields] AND "stroke"[MeSH]) OR ("cryptogenic stroke"[All Fields]) OR (Embolism of undetermined source[All Fields]) OR ("Embolism"[All Fields] AND "Stroke"[All Fields] AND "Undetermined"[All Fields] AND "Source"[All Fields]) OR ("ESUS"[All Fields]) OR OR OR OR OR OR OR OR OR OR) AND ((atherosclerosis[MeSH Terms]) OR "atherosclerosis"[All Fields]) OR (plaque, atherosclerotic[MeSH Terms]) OR ("plaque"[All Fields] AND "atherosclerotic"[All Fields]) OR "atherosclerotic plaque"[All Fields] OR "atheroma"[All Fields]) OR ("intraplaque"[All Fields] AND "hemorrhage"[All Fields]) OR ("intraplaque hemorrhage"[All Fields]) OR ("Lipid-rich necrotic core"[All Fields]) OR ("LRNC"[All Fields]) OR ("Lipid-rich"[All Fields] AND "Necrotic"[All Fields] AND "Core"[All Fields]) OR OR) AND ((aorta [MeSH]) OR (aorta [All Fields]) OR ("Aortic Valve"[MeSH]) OR ("Aortic"[All Fields] AND "Valve"[All Fields]) OR ("Aortic Valve"[All Fields]) OR ("Descending Aorta"[All Fields]) OR ("Descending"[All Fields] AND "Aorta"[All Fields]) OR ("Aortic Arch"[All Fields]) OR ("Aortic"[All Fields] AND "Arch"[All Fields]) OR ("Ascending Aorta"[All Fields]) OR ("Ascending"[All Fields] AND "Aorta"[All Fields]))</p> <p>Additional Filters using PubMed website:</p> <p>In the PubMed website, the following custom filters were applied to the results derived from above search strategy code: Humans, Adults 19+, 1/1/1980 – 12/05/2022, With Abstract, Article Type = Clinical Study, Clinical Trial, Phase I, II, III, IV, Comparative Study, Controlled Clinical Trial, Corrected and Republished Article, Evaluation Study, Observational Study, Pragmatic Clinical Trial, Preprint, Technical Report, Twin Study, Validation Study.</p>
<p>EMBASE Search Strategy Code</p> <p>(echocardiogram/exp OR 'echocardiogram:ab,ti OR 'tte' OR 'trans thoracic echocardiogram/de OR 'trans thoracic echocardiography/de OR ('trans thoracic' AND 'echocardiogram/de) OR 'tte':ab,ti OR 'computed tomography/exp OR 'ct'/de OR ('computed' AND 'tomography'/de) OR 'computed tomography':ab,ti OR 'mri'/exp OR 'magnetic resonance imaging'/de OR ('magnetic' AND 'resonance'/de AND 'imaging'/de) OR 'mri':ab,ti OR 'tee' OR 'transesophageal echocardiogram' OR 'transesophageal echocardiography'/de OR ('transesophageal' AND 'echocardiogram'/de) OR 'tee':ab,ti OR 'cta' OR 'computed tomography angiography' OR ('computed' AND 'tomography'/de AND 'angiography'/de) OR 'cta':ab,ti OR 'vessel wall imaging'/exp OR 'vwi' OR ('vessel wall'/de AND 'imaging'/de) OR 'vessel wall imaging':ab,ti OR 'spectral ct' OR 'spectral computed tomography'/de OR ('spectral' AND 'ct'/de) OR 'spectral ct':ab,ti OR 'vessel wall mr imaging' OR 'vessel wall mri' OR ('vessel wall'/de AND 'mri'/de) OR 'vessel wall mr imaging':ab,ti OR 'high resolution vessel wall mr imaging' OR 'high resolution vwi' OR 'hrvwi' OR ('high resolution' AND 'vessel wall'/de AND 'mri'/de) OR 'high resolution vessel wall mr</p>

imaging':ab,ti) AND ('infarction'/exp OR 'infarct'/exp OR 'infarction':ab,ti OR 'infarct':ab,ti OR 'cerebral artery disease'/exp OR ('cerebral' AND 'arterial' AND 'disease'/de) OR ('cerebral' AND 'artery'/de AND 'disease'/de) OR 'cerebral artery diseases':ab,ti OR 'arterial occlusive diseases'/exp OR ('arterial' AND 'occlusive' AND 'diseases'/de) OR 'arterial occlusive diseases':ab,ti OR 'stroke'/exp OR 'stroke':ab,ti OR 'brain ischemia'/exp OR ('brain'/de AND 'ischemia'/de) OR 'brain ischemia':ab,ti OR 'embolism'/exp OR 'embolism':ab,ti OR 'stroke etiology' OR ('stroke'/de AND 'etiology'/de) OR 'stroke etiology':ab,ti OR 'brain ischemia etiology' OR ('brain'/de AND 'ischemia'/de AND 'etiology'/de) OR 'brain ischemia etiology':ab,ti OR 'stroke diagnosis' OR ('stroke'/de AND 'diagnosis'/de) OR 'stroke diagnosis':ab,ti OR 'transient ischemic attack'/exp OR ('transient' AND 'ischemic' AND 'attack') OR 'transient ischemic attack':ab,ti OR 'brain ischemia diagnosis' OR ('brain'/de AND 'ischemia'/de AND 'diagnosis'/de) OR 'brain ischemia diagnosis':ab,ti OR 'cryptogenic stroke'/exp OR ('cryptogenic' AND 'stroke') OR 'cryptogenic stroke':ab,ti OR 'embolic stroke of undetermined source'/exp OR ('embolic' AND 'stroke'/de AND 'undetermined source') OR 'embolic stroke of undetermined source':ab,ti) AND ('atherosclerosis'/exp OR 'atherosclerosis':ab,ti OR 'plaque'/exp OR 'atherosclerotic' OR 'atheroma'/de OR ('atherosclerotic' AND 'plaque'/de) OR 'plaque':ab,ti OR 'intraplaque hemorrhage'/exp OR ('intraplaque' AND 'hemorrhage'/de) OR 'intraplaque hemorrhage':ab,ti OR 'lipid-rich necrotic core' OR 'lrnc' OR ('lipid-rich' AND 'necrotic core'/de) OR 'lipid-rich necrotic core':ab,ti) AND ('aorta'/exp OR 'aorta':ab,ti OR 'aortic valve'/exp OR ('aortic' AND 'valve'/de) OR 'aortic valve':ab,ti OR 'descending aorta'/exp OR ('descending' AND 'aorta'/de) OR 'descending aorta':ab,ti OR 'aortic arch'/exp OR ('aortic' AND 'arch') OR 'aortic arch':ab,ti OR 'ascending aorta'/exp OR ('ascending' AND 'aorta'/de) OR 'ascending aorta':ab,ti) AND ([adult]/lim OR [young adult]/lim OR [middle aged]/lim OR [aged]/lim OR [very elderly]/lim) AND ([embase]/lim OR [medline]/lim) NOT ([animals]/lim NOT [humans]/lim) AND ([article]/lim OR [article in press]/lim) AND [1-1-1980]/sd NOT [05-12-2022]/sd

Table S2: Article Inclusion/Exclusion Criteria for CAP Imaging Biomarkers by Imaging Modality

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> • Dates of publication: 1/1/1980 to 12/5/2022 • All languages • Prospective or retrospective • Humans • Used TEE, CT, MRI to assess for complex aortic plaque • Undetermined stroke source or ESUS* population for ischemic stroke • Adults (>18yo) • ≥10 cases in total ischemic stroke group • Assessed the aortic arch (Ascending/Arch/Descending) • Clinical observational studies, diagnostic accuracy studies, technical reports, reproducibility studies • *ESUS = no intracranial stenosis, <50% carotid stenosis, no coagulopathy, no malignancy, no cardiac history (no atrial fibrillation, arrhythmia, cardiac thrombus), no vasculitis 	<ul style="list-style-type: none"> • Animals, in vitro studies • Functional imaging (Nuclear Medicine) • Hemorrhagic stroke • Pediatric patients • <10 cases • Insufficient raw data; Must be able to isolate aortic patients if cohort is a mixed cohort. • Abdominal aorta, aortic valve • Narrative reviews, editorials, single case reports, conference abstracts • Special patient populations (e.g. sickle cell, von Willebrand disease, perioperative patients, trauma patients, valvular disease patients (e.g., endocarditis, valve prosthesis)) • Autopsy studies

Abbreviations: CAP, complex aortic plaque; ESUS, embolic stroke of undetermined source; TEE, transesophageal echocardiogram; CT, computed tomography; MRI, magnetic resonance imaging; CS, cryptogenic stroke.

Table S3: Article Inclusion/Exclusion Criteria for CAP Prevalence in Cryptogenic Stroke Patients

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> • Dates of publication: 1/1/1980 to 12/5/2022 • All languages • Prospective design • Humans • Used TEE, CT, MRI to assess for complex aortic plaque • Undetermined stroke source or ESUS* population for ischemic stroke • Adults (>18yo) • ≥10 cases in total ischemic stroke group • Assessed the aorta (Ascending/Arch/Descending) • Clinical observational studies, diagnostic accuracy studies, reproducibility studies • *ESUS = no intracranial stenosis, <50% carotid stenosis, no coagulopathy, no malignancy, no cardiac history (no atrial fibrillation, arrhythmia, cardiac thrombus), no vasculitis 	<ul style="list-style-type: none"> • Animals, in vitro studies (Cell Culture) • Functional imaging (Nuclear Medicine) • Hemorrhagic stroke • Pediatric patients • <10 cases • Insufficient raw data; Must be able to isolate aortic patients if cohort is a mixed cohort. In addition, must be able to isolate total number of patients with cryptogenic stroke and total number of patients with complex aortic plaque. • Focus is not in the thoracic aorta; abdominal aorta, aortic valve, aortic valve calcifications/sclerosis • Narrative reviews, editorials, single case reports, conference abstracts, technical reports • Special patient populations (e.g. sickle cell, von Willebrand disease, perioperative patients, trauma patients, valvular disease patients (e.g., endocarditis, valve prosthesis)) • Autopsy studies

Abbreviations: CAP, complex aortic plaque; ESUS, embolic stroke of undetermined source; TEE, transesophageal echocardiogram; CT, computed tomography; MRI, magnetic resonance imaging; CS, cryptogenic stroke.

Table S4: Modified Cochrane Collaboration Tool

Bias Type	Assessed Criteria
Selection Bias	<ul style="list-style-type: none"> • Did the study involve consecutive recruitment? • If not consecutive recruitment, was a random number generator used for inclusion of patients?
Performance Bias	<ul style="list-style-type: none"> • Were study participants and personnel blinded? • Were patients blinded to test results?
Detection Bias	<ul style="list-style-type: none"> • Were investigators obtaining images blinded to clinical outcome? • Were investigators interpreting images blinded to clinical data and to interpretations by other raters?
Attrition Bias	<ul style="list-style-type: none"> • Did the study clearly state exclusion criteria and number of patients excluded?
Reporting Bias	<ul style="list-style-type: none"> • Did the study report all prespecified outcomes from the reported methods?
Spectrum Bias	<ul style="list-style-type: none"> • Were stroke cases confirmed by diagnostic imaging, or by combination of clinical findings and diagnostic imaging? • Were additional sources of emboli excluded?

Table S5: Modified Guidelines for Reporting Reliability and Agreement Studies

Assessed Criteria
1. Did the study describe the time interval between repeated measurements?
2. Were study investigators measuring plaque blinded to clinical data?
3. Were study investigators measuring plaque blinded to stroke imaging data?
4. Did the study report interrater measures of plaque?
5. Did the study report intrarater measures of plaque?
6. Were the plaque measurements/ratings conducted independently?
7. Did the study describe methods of statistical analysis for reliability?
8. Did the study state the actual number of raters?
9. Did the study report the number of replicate observations that were conducted?
10. Did the study report characteristics of raters and subjects?
11. Did the study report experience (years) of raters?
12. Did the study report estimates of interrater reliability and agreement including measures of statistical uncertainty?
13. Did the study report estimates of intrarater reliability and agreement including measures of statistical uncertainty?

Table S6: Summary of Articles Included for CAP Imaging Biomarkers by Imaging Modality

Authors, Primary	Pro/retrospective	Imaging Modality for Aorta analysis	Evaluated Ascending Aorta	Plaque Thickness Threshold (mm)	Mobile component	Ulceration	Surface Irregularity	Hematomas/Thrombus
Tunick et al. ²¹	pro	TEE	Asc, Arch, Desc	5	1	0	0	0
Kessler et al. ²²	pro	TEE	Asc, Arch	5	1	0	0	0
Mendel et al. ²⁴	pro	TEE	Asc, Arch	5	0	1	0	0
Di Tullio et al. ²⁵	pro	TEE	Arch	4	1	1	0	0
Conti, A et al. ⁵⁰	pro	TEE	Not Reported	4	0	1	0	0
Viguier et al. ³⁹	pro	TEE	Asc, Arch	4	1	1	1	0
Cerrato et al. ³⁸	retro	TEE	Asc, Arch	4	1	1	1	0
Yahia et al. ³⁴	pro	TEE	Asc, Arch, Desc	4	1	1	0	1
Ward, R et al. ³²	retro	TEE	Asc, Arch, Desc	4	1	1	0	0
Dúbrava et al. ³¹	Pro	TEE	Asc, Arch	4	1	1	0	0
Petty et al. ⁶⁴	retro	TEE	Asc, Arch, Desc	4	1	1	0	0
Harloff et al. ³⁷	pro	TEE	Asc, Arch	4	1	0	1	1
Kaya et al. ⁴³	pro	CTA	Asc, Arch, Desc	4	0	1	0	0
Ko et al. ⁴¹	retro	CTA	Asc, Arch	4	0	1	0	1
Fujimoto et al. ⁵³	pro	TEE	Arch	4	1	1	0	0
Chatzikonstantinou et al. ⁴²	pro	TEE & CTA	Asc, Arch, Desc	NR	0	0	0	0
Harloff et al. ²⁸	pro	TEE & MRI	Asc, Arch, Desc	4	1	1	0	1
Kim, S et al. ¹⁹	pro	CTA	Asc, Arch, Desc	6	0	1	0	1
Chatzikonstantinou et al. ⁴⁵	pro	CTA	Asc, Arch, Desc	1	0	0	0	0
Jung et al. ¹⁶	retro	TEE	Asc, Arch	4	1	1	0	0
Shimada et al. ²⁹	pro	TEE	Arch, Desc	4	1	1	0	0
Ryoo et al. ⁴⁷	pro	TEE & CTA	Asc, Arch	4	1	1	0	0
Kim et al. ⁶⁵	retro	TEE	Asc, Arch, Desc	4	1	1	0	0
Wehrum et al. ⁹	pro	MRI	Asc, Arch, Desc	4	0	0	0	0
Ishizuka et al. ³⁰	retro	TEE	Arch	4	1	1	0	0
Mahfouz et al. ³³	pro	TEE	Asc, Arch	4	0	0	0	0
Ueno et al. ³¹	retro	TEE	Arch	4	1	1	0	0
Ntaios et al. ⁴	retro	TEE	Arch	4	1	1	0	0
Amarenco et al. ⁶⁶	pro	TEE	Asc, Arch, Desc	4	1	0	0	0
Mitusch et al. ²³	retro	TEE	Arch, Desc	5	1	0	1	1
Di Tullio et al. ¹⁸	pro	TEE	Asc, Arch, Desc	5	1	1	0	0
Rundek et al. ²⁶	pro	TEE	Arch	4	1	1	0	0
Castellanos et al. ²⁰	pro	TEE	Asc, Arch, Desc	4	1	1	0	0
Gupta et al. ⁶⁷	retro	TEE	Asc, Arch	4	1	1	0	0
Ko et al. ⁴⁰	retro	CTA	Asc, Arch	4	0	1	0	1
Haeusler et al. ⁸	pro	TEE & MRI	Arch	4	0	1	0	0
Umemura et al. ⁴⁶	retro	CTA	Arch	4	0	0	0	0
Mohammad et al. ⁴⁹	pro	TEE & MRI	Asc, Arch	4	0	0	0	0
Strecker et al. ³⁶	pro	TEE	Asc, Arch, Desc	4	1	0	0	1
Anan et al. ³²	pro	TEE	Arch	4	0	0	0	0
Morihara et al. ¹⁷	pro	TEE & MRI	Asc, Arch, Desc	4	0	0	0	0
Harloff et al. ³⁷	pro	TEE	Asc, Arch	4	1	1	0	1
Wehrum et al. ⁴⁸	pro	MRI	Asc, Arch, Desc	4	0	0	0	0
Gaspar et al. ⁶⁸	retro	TEE	Asc, Arch	4	0	0	0	0
Arun K et al. ⁴⁴	retro	CTA	Asc, Arch, Desc	4	0	1	0	0

Abbreviations: CAP, complex aortic arch plaque; NR, not reported; CS, cryptogenic stroke; CI, confidence interval; pro, prospective; retro, retrospective; Asc, Ascending aorta; Arch, Aortic arch; Desc, Descending aorta; 1/0, Evaluated/Not Evaluated.

Table S7: Summary of Articles Included for CAP Prevalence in Cryptogenic Stroke Patients

Authors	Year	Study Design	Number of Stroke Patients	Max number of patients with complex plaque	Modality	Aortic Segment Assessed	Plaque thickness Threshold (mm)	Mobile Plaque (1/0)	Ulceration (1/0)
Kessler et al. ²²	1996	cross-sectional	100	34	TEE	Asc, Arch	5	1	0
Di Tullio et al. ²⁵	1996	case control	40	15	TEE	Asc, Arch, Desc	5	1	1
Mendel et al. ²⁴	1998	cross-sectional	104	14	TEE	Asc, Arch, Desc	5	0	1
Rundek et al. ²⁶	1999	cross sectional	62	24	TEE	Arch	4	1	1
Conti et al. ⁵⁰	2000	cross-sectional	20	5	TEE	NR	4	0	1
Viguiet et al. ³⁹	2001	cross-sectional	40	14	TEE	Asc, Arch	4	1	1
Castellanos et al. ²⁰	2001	cross sectional	49	10	TEE	Asc, Arch, Desc	4	1	1
Yahia et al. ³⁴	2004	cross-sectional	237	79	TEE	Asc, Arch, Desc	4	1	1
Dúbrava et al. ⁵¹	2006	cross-sectional	218	29	TEE	Asc, Arch	4	1	1
Harloff et al. ²⁸	2006	cross sectional	212	37	TEE	Asc, Arch	4	1	1
Fujimoto et al. ⁵³	2011	cross sectional	127	80	TEE	Arch	4	1	1
Chatzikonstantinou et al. ⁴²	2012	cross sectional	64	21	TEE, CTA	Asc, Arch, Desc	NR	0	0
Kim et al. ⁶⁵	2012	cross sectional	63	15	CTA	Asc, Arch, Desc	6	0	1
Chatzikonstantinou et al. ⁴⁵	2012	cross sectional	71	22	CTA	Asc, Arch, Desc	1	0	0
Shimada et al. ²⁹	2013	cross sectional	178	74	TEE	Arch, Desc	4	1	1
Wehrum et al. ⁴⁸	2014	case control	67	31	MRI	Asc, Arch, Desc	4	0	0
Ryoo et al. ⁴⁷	2016	cross sectional	321	40†	TEE, CTA	Asc, Arch	4	1	1
Wehrum et al. ⁹	2017	case control	40	22	MRI	Asc, Arch, Desc	4	0	0
Haeusler et al. ⁸	2017	cross sectional	89	6‡	TEE, MRI	Arch	4	0	1
Mahfouz et al. ³³	2018	case control	56	40	TEE	Asc, Arch	4	0	0
Mohammad et al. ⁴⁹	2020	cross sectional	24	31	TEE, MRI	Asc, Arch	4	0	0
Strecker et al. ³⁶	2020	cross sectional	329	198	TEE	Asc, Arch, Desc	4	1	0
Anan et al. ⁵²	2021	cross sectional	267	147	TEE	Arch	4	1	0

†Data were aggregated based on TEE/CTA results.

‡ Data were aggregated based on 6 with TEE, 3 with MRI.

‡ Data were aggregated based on 3 with MRI, 1 with TEE.

Abbreviations: CAP, complex aortic arch plaque; NR, not reported; CS, cryptogenic stroke; CI, confidence interval; Asc, Ascending aorta; Arch, Aortic arch; Desc, Descending aorta; 1/0, Evaluated/Not Evaluated.

Figure S1: Funnel Plot to Assess Publication Bias

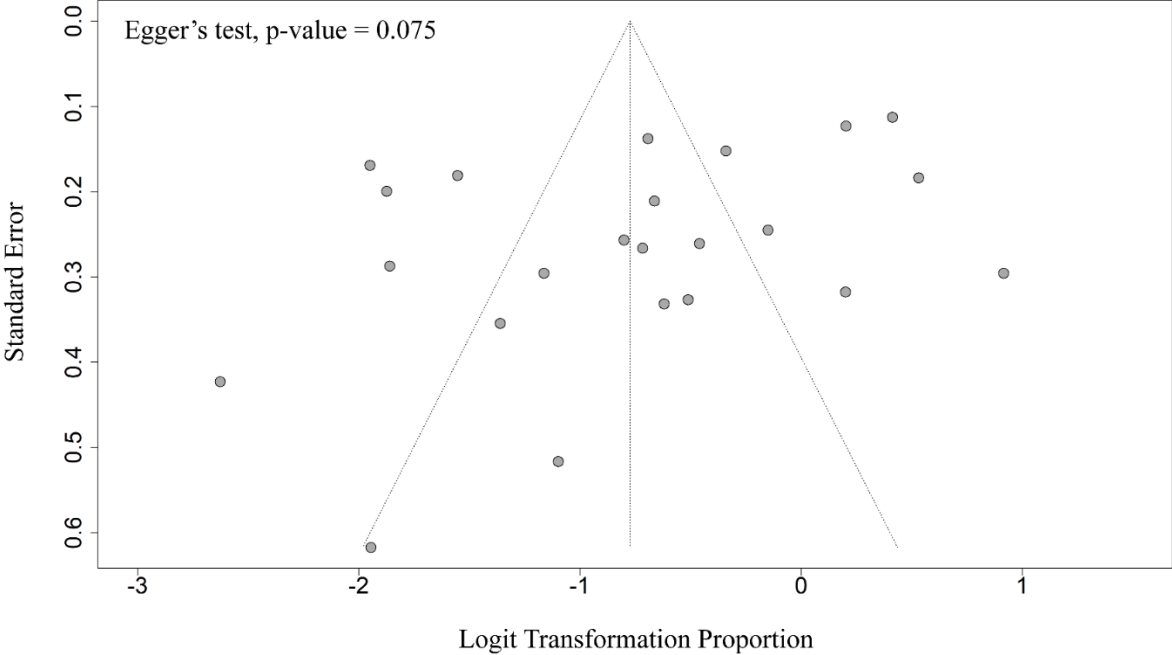
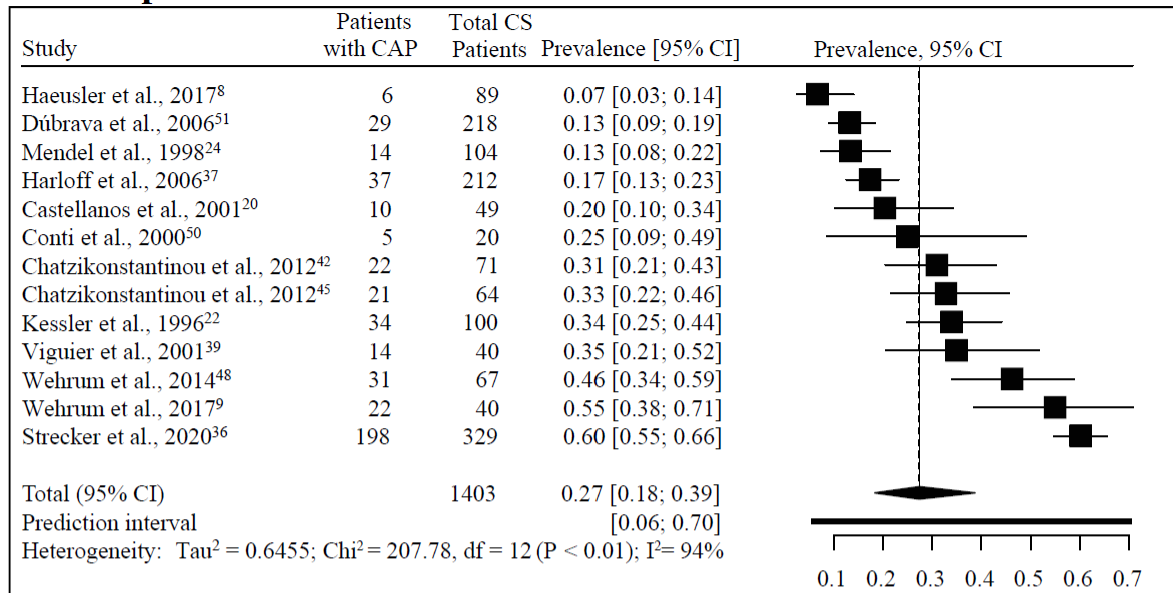
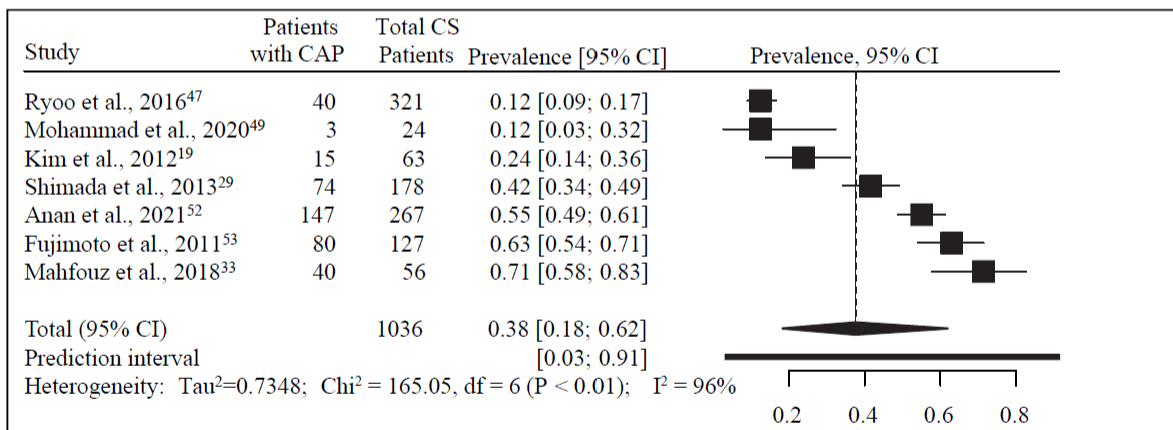


Figure S2: Subgroup-Analyses Based On Study Location

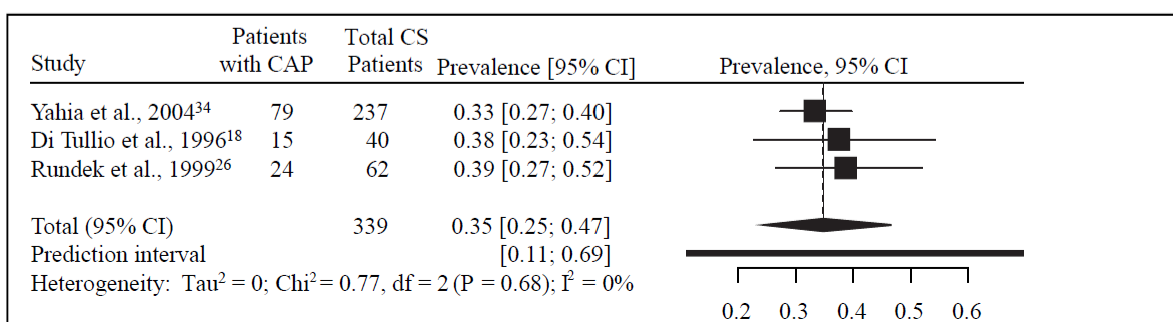
A. Europe



B. Asia



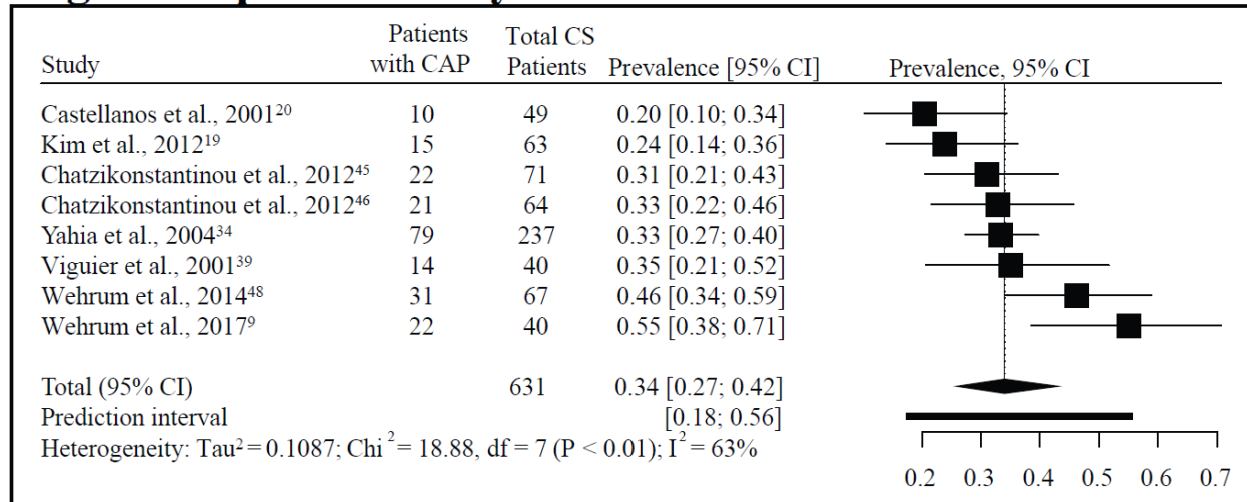
C. North America



Abbreviations: CAP, complex aortic plaque; CS, cryptogenic stroke; CI, confidence interval.

Figure S3: Subgroup-Analysis Based On Higher Reproducibility

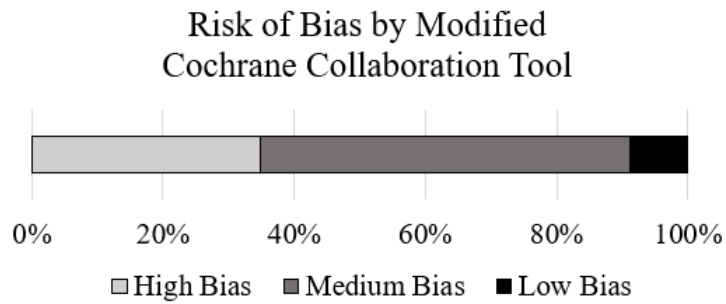
Higher Reproducibility Score



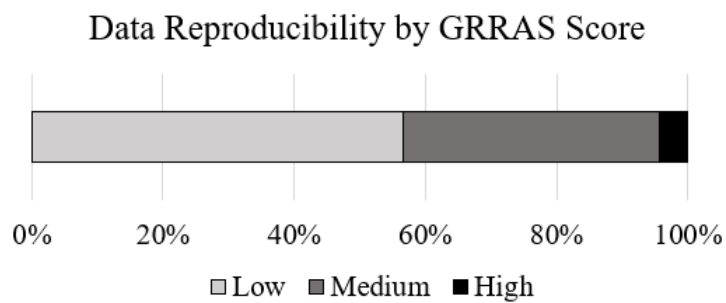
Eight studies were pooled to that met higher reproducibility scores (≥ 3 score based on the modified Guidelines for Reporting Reliability and Agreement Studies) and with at least 10 CS patients with CAP.

Abbreviations: CAP, complex aortic plaque; CS, cryptogenic stroke; CI, confidence interval

Figure S4: Risk of Bias and Reproducibility Reporting Assessment



Where "High Bias" is defined as scores in range [0,2], "Medium Bias" as [3,4], and "Low Bias" as [5,6]



Where "Low" is defined as scores in range [0,2], "Medium" as [3,6], and "High" as [7,12]

Assessments of risk of bias were performed using a modified Cochrane Collaboration Tool and modified version of the Guidelines for Reporting Reliability and Agreement Studies (GRRAS) checklist.

Supplemental Video Legends:

Video S1. Transesophageal echocardiogram movie of mobile plaque/thrombus in the ascending aorta. The mobile component measured approximately 1.34 x 0.627 cm as shown on the left-panel. Best viewed with Windows Media Player.

Video S2. Transesophageal echocardiogram movie of ulcerated plaque at the aortic arch with adjacent mobile components. Best viewed with Windows Media Player.