

Study Protocol

Title: Prevalence of Carotid Web in Youth Assessed by Duplex Sonography: a Cross-Sectional Study

Short Title: Carotid Web in Youth

Acronym: CaWY Study

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1) Background and Rationale

A carotid web (CaW) is a shelf-like, thin, triangular endoluminal projection—typically arising from the posterior wall of the internal carotid artery (ICA) bulb—considered by many to be an intimal variant of fibromuscular dysplasia and associated with embolic ischemic stroke in otherwise low-risk, younger patients. Although CT angiography (CTA) is most frequently used to diagnose CaW, characteristic appearances are detectable by carotid duplex ultrasound (DUS) on longitudinal B-mode with supportive Doppler findings; microflow/superb microvascular imaging can improve conspicuity. Population prevalence in the general young adult population is unknown; most estimates come from stroke cohorts ($\approx 2\%$ among symptomatic populations; higher within cryptogenic stroke subsets), so a dedicated, population-based sonographic study is needed.

2) Objectives and Hypotheses

Primary objective: Estimate point prevalence of carotid web in a general young adult population aged 15–25 years using duplex sonography.

Secondary objectives:

- Describe CaW laterality and morphology (web thickness, length, and projection angle) on ultrasound.
- Estimate prevalence of concomitant ICA/CCA atherosclerotic change or stenosis.
- Assess inter-observer agreement for CaW detection on DUS.
- In an adjudicated subset, compare DUS-suspected CaW with CTA (optional validation).

Hypothesis: Carotid web is present in 2 % of the general 15–25-year population (two-sided).

(This is a planning assumption; true prevalence may be lower/higher. Literature in symptomatic cohorts ranges roughly 2%, higher in cryptogenic stroke; general-population data are lacking.)

3) Study Design

Cross-sectional, multi-center, population-based sonographic survey with blinded central image adjudication, reported per STROBE guidelines for cross-sectional studies.

4) Study Population

Inclusion criteria

- Age 15 – 25 years at enrollment.
- Able to provide informed consent.

Exclusion criteria (for primary analysis; still recorded if present):

- Prior carotid endarterectomy/stenting, neck irradiation, or known vasculopathy with non-web lesions that preclude assessment.
- Inadequate acoustic window despite optimization (these participants contribute to feasibility metrics, not prevalence numerator/denominator).

Setting & sampling frame

- Community-based recruitment (secondary schools / universities).

- Stratified cluster sampling by sex, age bands (15-17, 18–21, 22–25), and recruitment site to approximate the underlying population.

5) Sample Size

Assumptions

- Expected prevalence $p=0.02$ (2%)
- Desired absolute precision $d=0.01$ ($\pm 1\%$)
- Confidence level 95% $\rightarrow Z=1.96$

Formula

$$n = \frac{Z^2 p(1-p)}{d^2} = \frac{1.96^2 \times 0.02 \times 0.98}{0.01^2} = 752.95$$

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Required minimum sample size: 753 participants (round up) plus 10% for non-diagnostic/poor-quality scans and no-shows, i.e. **totally 829 participants is needed to screen.**

6) Ultrasound Acquisition Protocol

Equipment & presets

- High-end ultrasound suplex machine Canon Aplio a-series with B-mode, color/power Doppler, spectral Doppler, and microflow/superb microvascular imaging. High-frequency linear transducer PLT-1005BT (5–14 MHz).
- Patient supine, slight neck extension/contralateral head rotation; optimize for the carotid bulb/ICA origin.

Scanning sequence (bilateral)

1. **B-mode:** transverse sweep from distal CCA through bulb into proximal ICA and ECA; then longitudinal (anterolateral, lateral, posterolateral windows).
2. **Color Doppler:** at low PRF to visualize flow separation/recirculation; adjust wall filter and gain to avoid overwriting thin intraluminal structures.
3. **Spectral Doppler:** with angle correction $\leq 60^\circ$, sample volume 1.5–2.0 mm; measure PSV and EDV in standard segments (distal CCA, bulb, proximal ICA).

4. **Microflow imaging:** focused on the posterolateral bulb to delineate thin shelf/membrane and adjacent flow.

Image storage

- Mandatory cine loops (≥ 3 cardiac cycles) in longitudinal and transverse of the bulb/ICA origin, plus still frames with and without color, and spectral Doppler waveforms with angle annotation ((same as in protocol of ANTIQUE study).
- Label side and projection; record machine make/model, probe, presets.

7) Sonographic Definition of Carotid Web

Definite carotid web:

Inclusion criteria:

1. Focal echogenic lesion in carotid bifurcation (15 mm proximally to flow divider and 15 mm distally)
2. The lesion is present (interferes) in the posterior wall
3. Echogenicity of the lesion is higher than intraluminal blood
4. Maximal length of lesions 3.0 mm
5. Minimal intraluminal prominence (width) 2.0 mm
6. In longitudinal view: Shape of lesion is shelf-like nor valve-like, triangular with the sharpest angle proximally with the blood flow direction
7. In transversal view: Transversal linear defect with echogenic surface projecting in the arterial lumen (the shape should be nest-like)
8. Hemodynamic signature: focal flow separation/recirculation or color aliasing immediately distal to the shelf without proportionate atherosclerotic plaque; spectral Doppler may be normal or show subtle focal acceleration without classic stenosis criteria.

Exclusion criteria:

1. The length is greater than the width
2. Visible only in transversal and not longitudinal view
3. Presence of carotid plaque (Mannheim consensus) in the posterior wall

Suspected carotid web:*Inclusion criteria:*

1. Focal echogenic lesion in carotid bifurcation (15 mm proximally to flow divider and 15 mm distally)
2. Minimal intraluminal prominence (width) 1.5 mm
3. One out of these criteria:
 - a. In longitudinal view: Shape of lesion is shelf-like nor valve-like, triangular with the sharpest angle proximally with the blood flow direction
 - b. In transversal view: Transversal linear defect with echogenic surface projecting in the arterial lumen (the shape should be nest-like)

Exclusion criteria:

1. Presence of carotid plaque (Mannheim consensus) in the posterior wall

Differential sonographic features to record: typical plaque (echogenic/heterogeneous with surface calcification), carotid diaphragm, dissection flap (mobile, intramural hematoma), carotid web with superimposed thrombus.

7) Sonographic Case Definition of Carotid Web

Required equipment/settings (if specified in your criteria):

- Probe / frequency: 5-14 MHz
- Settings: MI 1.6, 37 fps, Q scan, dynamic range 70
- Patient position: supine position, slight neck extension/contralateral head rotation

Diagnostic categories (tick all that apply):

- Definite CaW — must meet morphology, location, hemodynamics criteria and exclusions ruled out (plaque, dissection, diaphragm, artifact).
- Probable CaW — meets some morphology criteria and exclusions ruled out (plaque, dissection, diaphragm, artifact).

- Not CaW — meets no criteria for CaW.

Morphologic measurements (standardized):

- Web thickness (mm): ____ (measured at ____)
- Web length/projection into lumen (mm): ____
- Projection angle (°) relative to vessel wall: ____
- Distance from flow divider (mm): ____
- Side: left / right / bilateral

Hemodynamic signatures (as per your thresholds):

- Color Doppler recirculation/aliasing: present / absent (criteria: ____)
- Spectral Doppler acceleration: PSV ____ m/s (cutoff: ____); ICA/CCA ratio cutoff: ____
- Microflow imaging pattern: ____

Differential exclusion checklist (define image features to rule out):

- Atherosclerotic plaque: ____
- Dissection flap/intramural hematoma: ____
- Carotid diaphragm/other membranes: ____
- Artifact (reverberation, blooming): ____

Image acquisition minimums (per side):

- Transverse cine (≥ 3 cycles) focused on bulb/ICA origin
- Longitudinal cine in ≥ 2 insonation planes (lat & post-lat)
- Still frames (B-mode \pm color) with calipers for all measurements
- Spectral Doppler waveforms (CCA, bulb, proximal ICA) with angle correction $\leq 60^\circ$

Quality grading (apply your rules):

- Grade 1 (excellent) / 2 (diagnostic) / 3 (limited) — use only Grades 1–2 in primary analysis; Grade 3 in sensitivity analysis.

Reader guidance & adjudication using your criteria:

- Two blinded readers score Definite/Probable/Possible/Not CaW; discrepancies resolved by third reader under the same rubric.

- 10% repeat reads for κ /ICC.

CRF add-ons (pre-wired to your criteria)

- Checkboxes for each criterion element (present/absent/not evaluable).
- Auto-calculated category (Definite/Probable/Possible/Not CaW) based on boxes ticked.
- Mandatory image IDs linked to each measurement.

8) Training, Blinding, and Adjudication

- Sonographers undergo a standardized training module with exemplar images and checklists.
- **Blinding:** Operators are blinded to participant clinical data except age/sex; central readers (two expert neurosonologists) are blinded to site and each other.
- **Adjudication:** Disagreements (probable/possible/absent) resolved by a third senior reader.
- **Reliability:** 10% random sample re-read for inter-observer agreement (Cohen's κ for categorical calls; ICC for continuous measures).

9) Data Collection

- **Demographics:** age, sex, ethnicity (optional), height/weight.
- **Vascular risk factors:** smoking status, BP at visit, lipid profile if available, personal history of stroke/TIA/migraine, OCP use (females), recreational drugs, connective tissue disease/FMD history.
- **Ultrasound fields:** laterality; CaW category (absent/possible/probable), web dimensions (length, thickness, projection angle—estimate), distance from flow divider, presence of superimposed thrombus, plaque descriptors, standard velocities (CCA, bulb, ICA), ICA/CCA PSV ratio, EDV.
- **Imaging quality scores** and reasons for non-diagnostic studies.

10) Validation Substudy

- Participants with definite or possible CaW on DUS plus 1:2 matched DUS-negative controls (matched by age/sex/site) will invited for CTA within 4 weeks to evaluate concordance (index test: DUS; reference standard: CTA with thin-slice oblique sagittal reconstructions). Outcome: sensitivity/specificity and positive predictive value of DUS criteria. (CTA descriptions of CaW as thin, shelf-like posterior bulb defects guide the reference call.)

11) Outcomes

- **Primary:** Point prevalence of **probable CaW** (participants with ≥ 1 carotid web / all with diagnostic scans), with 95% CI adjusted for sampling design.
- **Secondary:**
 - Prevalence including **possible + probable** (sensitivity analysis).
 - Distribution by side (left/right/bilateral).
 - Association between CaW and sex, smoking, BP, OCP use (exploratory).
 - Inter-observer agreement metrics.
 - In validation substudy: DUS diagnostic accuracy vs CTA.

12) Statistical Analysis Plan

- **Weighting:** Apply sampling weights for cluster/strata to estimate population prevalence; robust SEs (Taylor linearization) or survey-design GLMs.
- **Descriptives:** Means/SDs or medians/IQRs; counts/% with 95% CIs.
- **Primary analysis:** Weighted prevalence and **exact (Clopper–Pearson) or Wilson** CIs for rare events; compare strata with Rao–Scott χ^2 .
- **Regression (exploratory):** Survey-weighted Poisson (log link, robust variance) for prevalence ratios of CaW vs candidate covariates.
- **Reliability:** Cohen’s κ with 95% CI (categorical), ICC(2,1) for continuous measures.
- **Missing data:** Report flow; use complete-case for primary prevalence; multiple imputation for covariate analyses if $>5\%$ missing.

- **Sensitivity analyses:** (i) include **possible** CaW as positive; (ii) restrict to scans with top quality scores; (iii) per-reader estimates.

13) Bias Minimization & Quality Control

- Pre-specified imaging protocol; machine presets harmonized across sites.
- Central training and periodic re-calibration; quarterly site audits of randomly selected studies.
- Consecutive sampling within clusters to reduce selection bias; track response rates.
- Maintain blinding; lock image sets before adjudication.

14) Ethics and Safety

- Minimal-risk imaging study; no ionizing radiation in the primary protocol.
- Informed consent; separate consent for optional CTA.
- Participants with **incidental significant carotid stenosis** or suspected thrombus receive counseling and referral per local care pathways.
- Data privacy per GDPR; coded IDs; secure storage.

15) Feasibility & Timeline

- **July-December 2025:** Finalize SOPs, train sonographers, pilot 50 scans to confirm criteria and quality metrics.
- **January 2026 – June 2026:** Enrollment and scanning.
- **May – June 2026:** Central reads and adjudication.
- **July – December 2026:** Analysis, manuscript preparation.

16) Case Report Forms (CRFs) — Core Fields (summary)

- **CRF-1 (Eligibility & Consent).**
- **CRF-2 (Demographics/Risk).**
- **CRF-3 (Ultrasound Acquisition):** device, probe, settings, windows obtained, quality.

- **CRF-4 (Ultrasound Findings):** CaW category; measurements; Doppler velocities; plaque; stenosis category; images saved (IDs).
- **CRF-5 (Adjudication):** reader A/B calls; consensus; κ .
- **CRF-6 (Validation Substudy):** CTA done (Y/N), CTA result (CaW Y/N), discordance reason.

17) Reporting

- Report per **STROBE**; include gallery of representative DUS images (longitudinal shelf-like lesion, transverse membrane, microflow swirl) and a flow diagram. Explicitly discuss limitations: web detection is operator-dependent; ultrasound criteria are less standardized than CTA; very low prevalence may limit precision without large samples.

Key References (for protocol justification)

1. **Fontaine L, et al.** *Ultrasound characteristics of carotid web*. J Neuroimaging. 2022. Describes B-mode/Doppler appearances; microflow imaging improves detection. ([PMC](#), [PubMed](#))
2. **Chen H, et al.** *Carotid webs: pathophysiology, diagnostic approaches, and management*. J NeuroIntervent Surg. 2024. Overview; ultrasound visualization best in longitudinal B-mode. ([jn.is.bmj.com](#))
3. **Radiopaedia (review).** *Carotid web*. Emphasizes shelf-like defect at posterior ICA bulb and CTA reference standard. ([Radiopaedia](#))
4. **Beach KW, et al.** *Standardized ultrasound evaluation of carotid stenosis*. 2010. Acquisition/measurement standards. ([PMC](#))
5. **SRU consensus criteria (summarized).** ICA PSV/EDV and ICA/CCA ratios for stenosis grading—context for standard carotid reporting alongside web detection. ([Radiopaedia](#))
6. **Yang T, et al.** *Prevalence and site of predilection of carotid webs (symptomatic cohort)*. Provides symptomatic/asymptomatic estimates within clinical samples. ([thejns.org](#))
7. **Sajedi PI, et al.** *Carotid Bulb Webs as a Cause of “Cryptogenic” Stroke*. 2017. Found shelves at posterior bulb in young stroke patients. ([PMC](#))