

Cover page

Full Title: Prevalence of carotid web in a French cohort of cryptogenic stroke.

Running title: Carotid webs prevalence in cryptogenic stroke.

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Abstract

Background and Purpose: Carotid webs (CaW) may be an under-recognized cause of anterior circulation cryptogenic ischemic stroke (ACIS). Prevalence is still unknown in European patients with ACIS.

Objective: To evaluate the prevalence of CaW in ACIS and describe patients with CaW phenotype in a cohort of patients from a French stroke center.

Methods: We conducted a retrospective monocentric cohort study from 01/01/2015 to 31/12/2019 (Montpellier University Hospital, France), in consecutive anterior ischemic stroke (AIS) patients ≤ 65 years old from a prospective stroke database. Using ASCOD phenotyping, ACIS patients were selected and cervical CTA were reviewed to find CaW.

Results: Among 1053 consecutive AIS patients, 266 ACIS patients with CTA were included. Among patients included (mean age 50, women 58%), CaW was in the ipsilateral carotid (iCaW) in 21 patients: 7.9% (95%CI [4.6-11.1]), (mean age 51, 11 women, 16 Caucasian). iCaW were uncovered during study review of CTA in 6/21 (29%) patients. Comparison between patients with iCaW and those without iCaW showed no differences except that of a higher rate of intracranial large vessel occlusion (LVO) (62.4 vs 37.6%; $p = 0.03$). Patients with iCaW under conservative medical therapy had an annualized stroke recurrence rate (SRR) of 11.4% (95%CI [8.4-15.1]).

Conclusions: iCaW was identified as a source of stroke in about 8% of a French population ≤ 65 years with ACIS. iCaW was associated with a higher rate of LVO and a high SRR under conservative medical therapy.

Keywords: Cryptogenic strokes; embolic stroke of undetermined source; Carotid diaphragm;
Carotid web

Introduction:

Carotid webs (CaW) may be an under-recognized source of anterior circulation cerebral infarct or transient ischemic attack (TIA). CaW ipsilateral to stroke (iCaW) prevalence ranges from 8% to 37% of young patients with anterior circulation cryptogenic ischemic stroke (ACIS) from a few monocentric studies¹⁻⁵, and 9% of unselected TIA patients in a retrospective cohort from China⁶. However, patients with ACIS from previous published series were mainly of African ethnicity from North America^{1,2,4} and the French west indies³. In European native populations with ACIS, prevalence of iCaW is still little described and has been reported in around twenty white or Caucasian patients to date^{5,7,8}. In a recently updated systematic review of CaW associated with stroke by Olindo et al.⁹, patients with iCaW were Caucasian in only 13.8% of 189 published cases and a mean prevalence of iCaW in cryptogenic stroke patients of 12.7%. ICaW was found in 2.5% of patients included in the MR CLEAN Trial¹⁰, which recruited patients with anterior circulation ischemic stroke (AIS), however, ethnicity was not specified. Labeyrie et al.⁵ found a higher prevalence of iCaW in a small population of patients with an embolic stroke of undetermined source (ESUS) (n= 6/56, 10.7%) than in the non-ESUS group (n= 3/410, 0.7%). However, in both studies, all patients had intracranial large vessel occlusion (LVO).

Diagnosis of CaW is both critical and challenging, because CaW is associated with a high rate of ipsilateral recurrent stroke (up to 30-50% of patients under conservative medical therapy^{7,11}) and prevention of recurrence by surgery or stenting seem promising¹¹⁻¹³. The objective of this study was to describe the prevalence of CaW and phenotype of patients with CaW among a young population with ACIS admitted to a comprehensive stroke center in France.

Methods:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Population. The study was approved by the local ethics committee (Institutional Review Board of Montpellier University Hospital) under number 2018_IRB-MTP_06-06. Patients admitted to the stroke unit of the comprehensive stroke center of Montpellier or proxy are informed of academic work and consent orally that their data may be used in a Stroke database for clinical research purposes.

We performed a retrospective monocentric study with data extraction from our prospective clinical registries of consecutive patients admitted for cerebral infarction to the stroke unit of Montpellier's Academic Hospital, France, between January 2015 and December 2019.

Patients were included if they fulfilled the following criteria: 1) age \leq 65 years-old; 2) AIS; 3) cryptogenic ischemic stroke after an extensive etiological workup based upon current guidelines and local protocol; and 4) exploration of cervical and intracranial carotid artery with computed tomography-angiography (CTA).

Given its high accuracy in previous studies^{11,12,14} and in order to minimize the risk of false negative for CaW detection during screening, we chose to build CaW prevalence evaluation by reviewing consecutive ACIS patients explored with CTA, excluding patients explored with MRA only. A comparison analysis between ACIS patients not explored with CTA (n= 126) and included patients (n=266) was planned (supplemental table 1).

We restricted our study to patients with an age \leq 65 years-old to ensure a low probability of coexisting covert paroxysmal atrial fibrillation compared to older patients among a population with ESUS. In addition, previous compiled literature data and our preliminary local clinical experience suggested an average age of about 50 at diagnosis of stroke associated with CaW

and would indicate a rather infrequent association between cryptogenic stroke and CaW in older patients, although possible.

Etiological workup was standardized in all ACIS patients. Cardiac investigations included transthoracic and transesophageal echography (if transthoracic was normal), and at least 24-hour in-hospital continuous cardiac monitoring and 24-hour Holter outpatient recording. Comprehensive laboratory tests were performed, including antiphospholipid antibodies and urinary toxic screening in all patient ≤ 60 y.o., and further thrombophilia or immunologic tests when required according to clinical judgment and patient medical history. Systematic cervical and brain CTA and/or gadolinium magnetic resonance imaging angiography (MRA), completed when warranted with a Doppler ultrasound carotid echography to precise or confirm unusual findings (such as non-stenosing complex atherosclerotic plaque, CaW suspicion, mural thrombus...) on cervical carotid wall arteries on MRA or CTA.

After this work-up, stroke etiology was defined according to ASCOD¹⁵ phenotyping classification, also fulfilling “ESUS” criteria¹⁶. Patients with a causality assigned “1” (if the disease is present and can potentially be a cause) were excluded. Patients with patent foramen ovale or atrial septal defect were included (causality “2”, causality link is uncertain). Ethnicity was based upon self-identification.

Diagnosis of CaW. All CTAs were initially reviewed by one neuroradiology resident (FLC) and one experienced neuroradiologist (CD). Protocol of CTAs can be found in the appendix. The presence of a CaW was established using a baseline assessment, and was confirmed on follow-up CTA when dubious. CaW was diagnosed when consensus was obtained from 4 readers: neuroradiologist (FLC, CD), one neurology resident (CT) and one experienced stroke neurologist (NG). Criteria for identification of the CaW were evaluated on axial and oblique sagittal, two-dimension reconstructions: thin and smooth membrane-like intraluminal defect originating from the posterior wall of the carotid bulb on sagittal oblique reconstructions, with

a corresponding septum-like image on axial reconstructions^{11,14}. Differential diagnosis included atherosclerotic plaques, carotid artery dissection, thrombus of lesion free carotid, inflammatory stenosis, and small protruding lesions as defined by Choi et al¹⁴. The lengths of the CaW were measured according to Haussen et al.¹², and the degree of carotid stenosis was calculated using NASCET (North American Symptomatic Carotid Endarterectomy Trial)¹⁷ criteria.

A concordance analysis was performed to assess the reproducibility of CaW suspicion by readers with the use of an interobserver agreement evaluation between 5 readers: the 4 aforementioned readers and one independent neuroradiologist (ID). A pool of 50 CTAs with axial and sagittal oblique reconstructions was selected and anonymized, including 5 diagnosed CaW, 5 internal carotid artery spontaneous dissections, 20 carotid bulb atherosclerotic plaques, and 20 normal appearing arteries.

Data collection. Data were prospectively collected by the stroke neurologist: 1) Patient characteristics: demographics (age, sex, ethnicity), past medical history, medication, cardiovascular risk-factors (smoking, hypertension, diabetes, dyslipidemia, vascular history), initial and final NIHSS, and 3 months modified Rankin scale; 2) stroke imaging : type of initial imagery, presence and localization or absence of occlusion, and stroke localization; 3) initial treatment; 4) relevant biological results; and 5) Follow-up parameters (stroke recurrences, NIHSS, modified Rankin scale, treatment). Neuroradiologists collected CaW characteristics (length, NASCET, presence or absence of thrombus) by reviewing the CTA.

Statistical analysis. Descriptive data and clinical information were presented as proportion for qualitative variables, as means and interquartile intervals for quantitative data.

Comparison between patients with and without CaW were assessed using the Mann-Whitney U test for quantitative data, and Fisher's exact test and Chi-2 test for qualitative data. A logistic

regression with a stepwise selection procedure was performed to estimate OR in a multivariate model. Statistical significance was defined as $p \leq 0.05$.

Results

Prevalence of CaW and description of the studied population

Among 1053 consecutive patients ≤ 65 years old with AIS, 392 had ACIS, of whom 266 patients with CTA were included. Flow chart (figure 1) and supplemental table 1 present the selection and characteristics of these 266 patients. The planned comparison analysis between ACIS patients not explored with CTA, and patients included in the present study, show that people without CTA were older (54.1 vs 50.4, $p < 0.01$). Proximal occlusion was more frequent in the group of patients explored with CTA (supplemental Table 1). In the concordance analysis CaW were all correctly diagnosed. Kappa coefficient was 0.92 ($p < 0.0001$; according to Fleiss's Kappa methods).

Among the 266 ACIS patients, 24 patients had a CaW (9.02%), ipsilateral to the AIS in 21 cases, contralateral in 3, and bilateral in 4. Overall, iCaW to stroke was found in 21/266 patients, indicating a prevalence of 7.89% (95%CI [4.65-11.14]), compared to 2.63% ($n=7/266$; 95%CI [0.71-4.56]) on the contralateral side (OR 3.16; 95%CI [1.27-8.97], $p < 0.01$). iCaW was uncovered during CTA review for this study in 6/21 patients (29%).

Main characteristics of ACIS patients with or without iCaW are presented in table 1.

Univariate (table 1) comparison showed no significant differences except patients with iCaW had a proximal intracranial occlusion more often (62.4 vs 37.6%; $p = 0.03$). Among group of patients with ACIS and intracranial LVO only ($n=132$ patients), 14 patients had iCaW, 13.5% (95%CI [7.4-22.6]).

Phenotype of patients with iCaW

Detailed description of the 21 patients with iCaW is provided in Table 2 and CaW imaging is illustrated in Figure 2. Sixteen patients were Caucasian, 3 were Middle Eastern, 1 Asian, and 1 mixed Black-African and Caucasian. Among these 21 iCaW patients, 4 had bilateral CaW. The mean length of CaW was 3.1 mm (IQR 2.47-3.45). The mean degree of carotid stenosis

(NASCET) was 6%. An intracranial proximal artery occlusion (M1 or M2 segments of the middle cerebral artery) ipsilateral to CaW was found in 13/21 (62.4%). Six out of 21 patients had thrombus trapped in CW during acute stroke management on imaging. Four patients received anticoagulation by heparin, 1 patient dual antiplatelet therapy and one patient had a stenting during acute stroke management. Five out of 6 had control CTA, performed between 1 to 3 weeks after antithrombotic therapy initiation, which showed complete regression of thrombi; the last one patient received anticoagulation because of intracranial occlusion during acute stroke but control cervical CTA was performed later after retrospective diagnosis.

Treatment and follow-up of patients with iCaW.

All iCaW patients received antiplatelet therapy after first IS, and 5 received short term anticoagulation therapy in addition. One patient was lost to follow-up, 4/20 patients had at least one stroke recurrence (20%) before CaW stenting or last medical follow-up if under conservative medical therapy only (table 2). The annualized recurrence rate under conservative medical therapy was 11.4% (95% CI [8.4-15.1]). All other iCaW patients had no recurrences after a mean follow-up of 24 months [4-55]). Fourteen out of 21 iCaW patients underwent carotid angioplasty with stenting (66.7%) without any symptomatic stroke during procedure or follow-up (mean follow up 10.6 months [0-36]). Among 14/21 patients treated with stenting, 5 were treated beyond 2 months after first IS. Among those, 2 had a retrospective diagnosis of CaW during study review; 2 had a diagnosis of CaW after second IS occurred; 1 had a diagnosis of CaW during follow-up 11 months after IS.

There was no significant statistical relationship between the degree of stenosis or CaW length and the severity of stroke (NIHSS score on admission, presence of LVO) or recurrence of IS.

Discussion

Our study is one of the first and largest to estimate the prevalence of CaW associated with ACIS among a European continental population, mostly originating from Caucasian ethnicity. The prevalence of 8% for CaW associated with ipsilateral ACIS is in the lower range of iCaW prevalence from previous similar cohort studies which ranged from 8 % to 37%^{1-4,12}.

We hypothesize that heterogeneity of iCaW prevalence in ACIS patients is presumably linked to ethnicity origin differences among stroke populations, although debatable. Indeed, other main demographic and stroke patients' characteristics between cohorts appear comparable and homogeneous. In previous published studies, CaW typically affects middle-aged adults, predominantly Afro-American or Afro-Caribbean women, with low rates of usual atherosclerotic risk factors^{7,8,11}. Based on previous systematic review⁹, ethnic information was available in about half of the patients described in monocentric case series, mainly originating from north America and the French West Indies, where many people are of Black African descent^{1-4,14}: Black African descendants accounted for 60% of cases, 25% were Asiatic and 14% Caucasian. Other explanations leading to a lower prevalence of iCaW in our study may be a higher cut-off age than in other comparable cohorts^{1-4,12}.

To date, two studies in Europe have attempted to estimate CaW prevalence. The first is a retrospective review of CTA from 443 AIS patients included in the MR Clean Trial conducted in The Netherlands. iCaW was found in 2.5% of patients. However, the lower CaW prevalence in this study is not fully comparable to our cohort of patients or other previous cohorts^{1-4,12}: firstly, only patients with an intracranial proximal occlusion were included; secondly, the study didn't include exclusively young patients with cryptogenic AIS. The other study was conducted in France by Labeyrie et al⁵ in a population of LVO stroke patients selected from a thrombectomy stroke database. They found ipsilateral CaW to be more frequent in ESUS than in the rest of the sample (10.7% (confidence interval 95% [2.7–18.7]

vs. 0.7% (0–1.5), $P < 0.001$), suggesting a causality link between iCaW and ESUS. Our results are consistent with Prevalence estimation of iCaW in this latter study.

CaW can easily be missed with CTA even by neurologists or radiologists skilled in stroke management, or misdiagnosed especially when a thrombus is lodged in the CaW. Confirming our study-hypothesis, the review of all CTA allowed us to uncover a previously missed CaW in a third of patients with ACIS associated with CaW in the present cohort. In line with other studies^{10,18}, we demonstrated a high interobserver agreement (k , 0.92), another advantage of CTA for CaW diagnosis. We therefore suggest that a CTA with multiplanar reconstructions, in place or in addition to MRA and Doppler ultrasound carotid echography, unless contraindicated, should be performed systematically to unmask a possible web in ACIS patients, especially in young AIS patients or those without any major cardiovascular risk factors.

Our study provides new insights towards CaW patients phenotype since our case series from a French continental cohort, with a high representation of Caucasian patients, share similar profiles as AIS patients described from America or the French west Indies, mostly Black African descendants^{7,8}. Our CaW patients had less frequent, but not significantly, cardiovascular risk factors than those without CaW, although age was similar. Most important, about two-thirds of ACIS with iCaW in our cohort presented with proximal (M1 or M2 segments of the middle cerebral artery) intracranial occlusion, and we found a rate of LVO almost twice as frequent as the one of ACIS patients without iCaW. Again, our results are consistent with those of the Haussen et al.¹² series where 52% of 24 iCaW patients received mechanical thrombectomy (although the intracranial occlusion site was not detailed) and with the Kim study⁴ from Atlanta study group too, where proximal occlusions were more frequent in patients with CaW (100% vs 55%). When iCaW prevalence calculation in our cohort was restricted to ACIS patients with LVO only, it rose to 13.5% (95% CI 7.4-22.6%), close to the prevalence of 10,7% found by Labeyrie et al.⁵

Accurate and early diagnosis of CaW is crucial, given the very high rate of ipsilateral stroke recurrence under conservative medical treatment (antiplatelet therapy or anticoagulation) as found in our cohort and close to previous convincing estimates^{7,11}, and is amenable to probable safe and efficient preventive treatment with endovascular stenting or surgical excision^{7,12}. Indeed, we observed a high stroke recurrence rate with 4 patients under medical therapy out of 20 during follow-up who suffered from at least one recurrent stroke or TIA ipsilateral to CaW within a period of 21 months, 3 of them during first year, resulting in an estimated SRR close to 11% per year. This striking high SRR in a cohort of young patients with few risk factors is similar to findings in Afro-Caribbean's patients by Joux et al.¹¹, who reported an average SRR of 12% per year during a follow of 3 years among patient under medical therapy, with the highest rate during the first year, which was as high as 20-25%^{7,11}. As a comparison, estimated average annualized stroke rate under antiplatelets therapy was 1% per year among young French patients with cryptogenic stroke associated with PFO¹⁹, and 4.5% per year among ESUS patients^{20,21}. As previously described¹², in our cohort all embolic recurrences occurred under antiplatelets therapy only and no recurrence was observed after CaW stenting, safely performed in 14 patients.

The main limitations of our study are a monocentric tertiary hospital-based prevalence calculation with retrospective design, a lack of proven histology of suspected CaW, and about a third of patients were excluded for lack of CTA. However, our comparison analysis shows they shared similar characteristics with studied patients, except a slight difference in age and frequency of proximal occlusion. It may reflect local acute stroke imaging protocol favoring the use of CTA over MRA. Another explanation is that we decided to do a systematic CTA exploration for young patients since 2017, even with normal appearing first-line MRA to prevent CaW under-detection, as discussed above. Also, our population with CaW contains patients with multiple ethnicities, which likely reflects mix ethnicities of people living in the

Montpellier City area, although a vast majority of patients were Caucasian and only one patient had a Black-African ethnicity parent. Because this work was designed to study carefully selected cryptogenic strokes or ESUS patients, we lack information about CaW prevalence either among non-cryptogenic stroke or among the general population. Those data are needed to improve our understanding of stroke related to CaW and thus deserves further future research.

Conclusion

CaW ipsilateral to ACIS in patients ≤ 65 years from a French continental, mostly Caucasian ethnicity population, was found in about 8% of consecutive cases and 13.5% of patients with LVO. This rate is lower than previous Caribbean or North American cohorts including a high proportion of Black-African descendants, however, our patients had similar main characteristics at presentation and during follow-up. Given assumed high recurrence rate of stroke associated with CaW and specific management, its recognition is crucial and systematic neck CTA should be carefully considered in work-up of ACIS patients, from any ethnicity, to reduce risk of undetection of iCaW.

References

1. Sajedi PI, Gonzalez JN, Cronin CA, Kouo T, Steven A, Zhuo J, et al. Carotid Bulb Webs as a Cause of “Cryptogenic” Ischemic Stroke. *American Journal of Neuroradiology*. 2017 Jul;38(7):1399–1404.
2. Coutinho JM, Derkatch S, Potvin ARJ, Tomlinson G, Casaubon LK, Silver FL, et al. Carotid artery web and ischemic stroke: A case-control study. *Neurology*. 2017 Jan 3;88(1):65–69.
3. Joux J, Boulanger M, Jeannin S, Chausson N, Hennequin J-L, Molinié V, et al. Association Between Carotid Bulb Diaphragm and Ischemic Stroke in Young Afro-Caribbean Patients: A Population-Based Case–Control Study. *Stroke*. 2016 Oct;47(10):2641–2644.
4. Kim SJ, Allen JW, Bousslama M, Nahab F, Frankel MR, Nogueira RG, et al. Carotid Webs in Cryptogenic Ischemic Strokes: A Matched Case-Control Study. *Journal of Stroke and Cerebrovascular Diseases*. 2019 Sep;104402.
5. Labeyrie M-A, Serrano F, Civelli V, Jourdaine C, Reiner P, Saint-Maurice J-P, et al. Carotid artery webs in embolic stroke of undetermined source with large intracranial vessel occlusion. *Int J Stroke*. 2020;
6. Hu H, Zhang X, Zhao J, Li Y, Zhao Y. Transient Ischemic Attack and Carotid Web. *American Journal of Neuroradiology*. 2019 Feb;40(2):313–318.
7. Zhang AJ, Dhruv P, Choi P, Bakker C, Koffel J, Anderson D, et al. A Systematic Literature Review of Patients With Carotid Web and Acute Ischemic Stroke. *Stroke*. 2018 Dec;49(12):2872–2876.
8. Kim SJ, Nogueira RG, Haussen DC. Current Understanding and Gaps in Research of Carotid Webs in Ischemic Strokes: A Review. *JAMA Neurol*. 2019 Mar 1;76(3):355–361.

9. Olindo S, Marnat G, Chausson N, Turpinat C, Smadja D, Gaillard N (2021). Carotid webs associated with ischemic stroke. Updated general review and research directions., *Rev Neurol (Paris)*. 2021 Jan 14:
10. Compagne KCJ, van Es ACGM, Berkhemer OA, Borst J, Roos YBWEM, van Oostenbrugge RJ, et al. Prevalence of Carotid Web in Patients with Acute Intracranial Stroke Due to Intracranial Large Vessel Occlusion. *Radiology*. 2018 Mar;286(3):1000–1007.
11. Joux J, Chausson N, Jeannin S, Saint-Vil M, Mejdoubi M, Hennequin J-L, et al. Carotid-Bulb Atypical Fibromuscular Dysplasia in Young Afro-Caribbean Patients With Stroke. *Stroke*. 2014 Dec;45(12):3711–3713.
12. Haussen DC, Grossberg JA, Bousslama M, Pradilla G, Belagaje S, Bianchi N, et al. Carotid Web (Intimal Fibromuscular Dysplasia) Has High Stroke Recurrence Risk and Is Amenable to Stenting. *Stroke*. 2017 Nov;48(11):3134–3137.
13. Haussen, Diogo C., Jonathan A. Grossberg, Sebastian Koch, Amer Malik, Dileep Yavagal, Benjamin Gory, Wolfgang Leesch, et al. 2018. « Multicenter Experience with Stenting for Symptomatic Carotid Web ». *Interventional Neurology* 7: 413-18.
14. Choi PMC, Singh D, Trivedi A, Qazi E, George D, Wong J, et al. Carotid Webs and Recurrent Ischemic Strokes in the Era of CT Angiography. *American Journal of Neuroradiology*. 2015 Nov;36(11):2134–2139.
15. Amarenco P, Bogousslavsky J, Caplan LR, Donnan GA, Wolf ME, Hennerici MG. The ASCOD Phenotyping of Ischemic Stroke (Updated ASCO Phenotyping). *Cerebrovascular Diseases*. 2013;36(1):1–5.
16. Hart RG, Diener H-C, Coutts SB, Easton JD, Granger CB, O'Donnell MJ, et al. Embolic strokes of undetermined source: the case for a new clinical construct. *Lancet Neurol*. 2014 Apr;13(4):429–38.

17. Barnett HJM, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB, et al. Benefit of Carotid Endarterectomy in Patients with Symptomatic Moderate or Severe Stenosis. *N Engl J Med.* 1998 Nov 12;339(20):1415–25.
18. Madaelil TP, Grossberg JA, Nogueira RG, Anderson A, Barreira C, Frankel M, et al. Multimodality Imaging in Carotid Web. *Front Neurol.* 2019;10:220.
19. Mas J-L, Derumeaux G, Guillon B, Massardier E, Hosseini H, Mechtouff L, et al. Patent Foramen Ovale Closure or Anticoagulation vs. Antiplatelets after Stroke. *N Engl J Med.* 2017 14;377(11):1011–21.
20. Hart Robert G., Catanese Luciana, Perera Kanjana S., Ntaios George, Connolly Stuart J. Embolic Stroke of Undetermined Source. *Stroke.* 2017 Apr 1;48(4):867–72.
21. Diener H-C, Sacco RL, Easton JD, Granger CB, Bernstein RA, Uchiyama S, et al. Dabigatran for Prevention of Stroke after Embolic Stroke of Undetermined Source. *New England Journal of Medicine.* 2019 May 16;380(20):1906–17.

Figure 1: Patients selection flow chart

Figure 2: CTA, oblique sagittal views, of a right carotid web. Image A, carotid web with superimposed thrombus. Image B, migration of the thrombus (embolic ischemic stroke in M1 right artery) after 7 days of anticoagulation, revealing the carotid web. Image C, axial view, left carotid web with “impression of 3 lumen”. Image D, lateral view of 3D reconstruction of the carotid web. Images E and F, angiography, lateral view, with posterior defect of the left internal carotid (E) and stagnation of contrast (F).

Table 1: Comparison of patients with carotid web (CaW) ipsilateral (iCaW) to ischemic stroke and patients without ipsilateral CaW.

Table 2: Clinical and radiological description of patients with carotid web ipsilateral to ischemic stroke

Online data supplement:

Supplemental table I : Characteristics of patients included compared to patients without angio-CT scanner available

Abbreviations

ACIS: anterior circulation cryptogenic ischemic stroke

AIS: anterior circulation ischemic stroke

CTA: CT-angiography

CaW: carotid web

iCaW: carotid web ipsilateral to stroke

MRA: magnetic resonance imaging angiography

TIA: transient ischemic attack

Figure 1

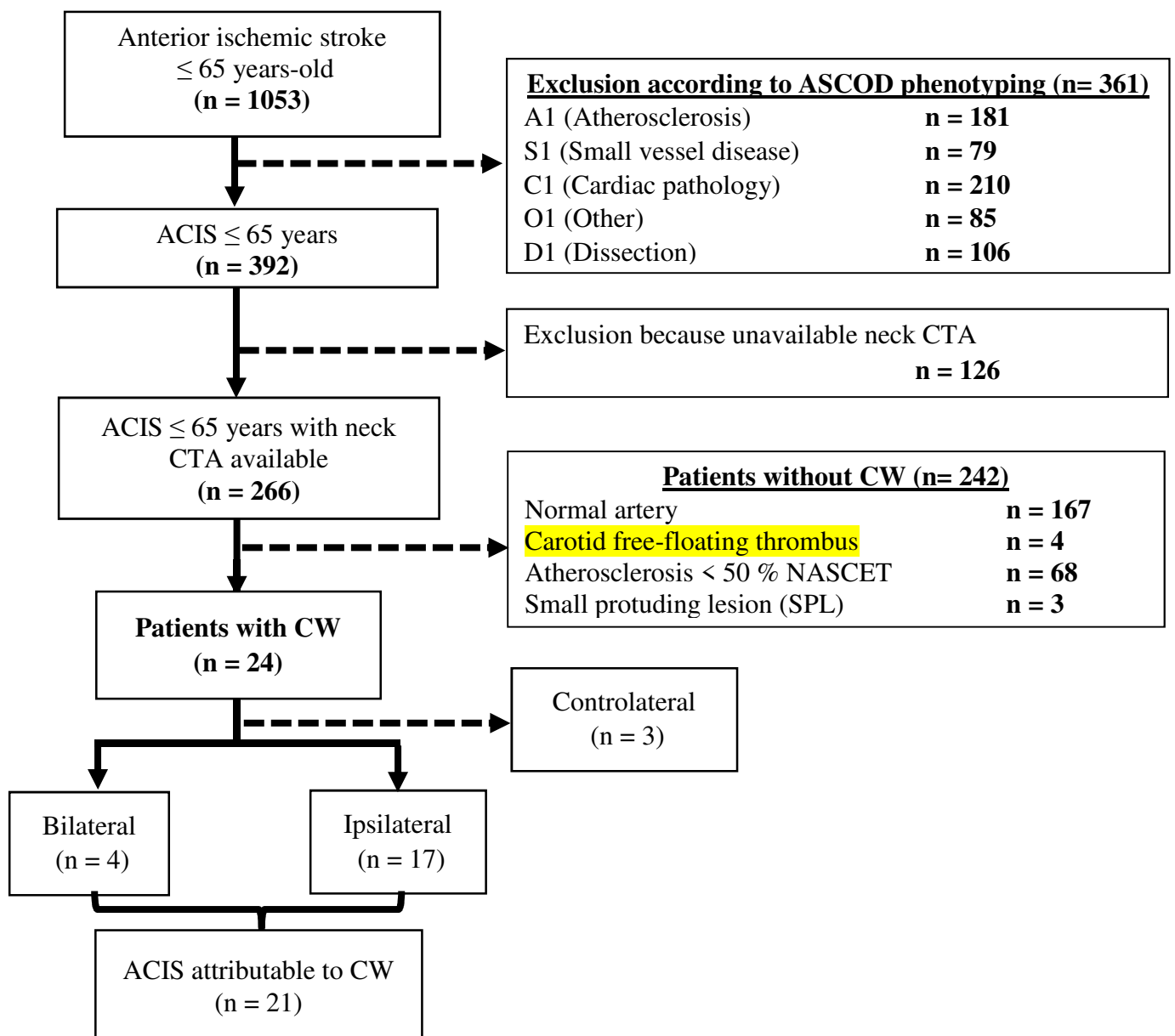
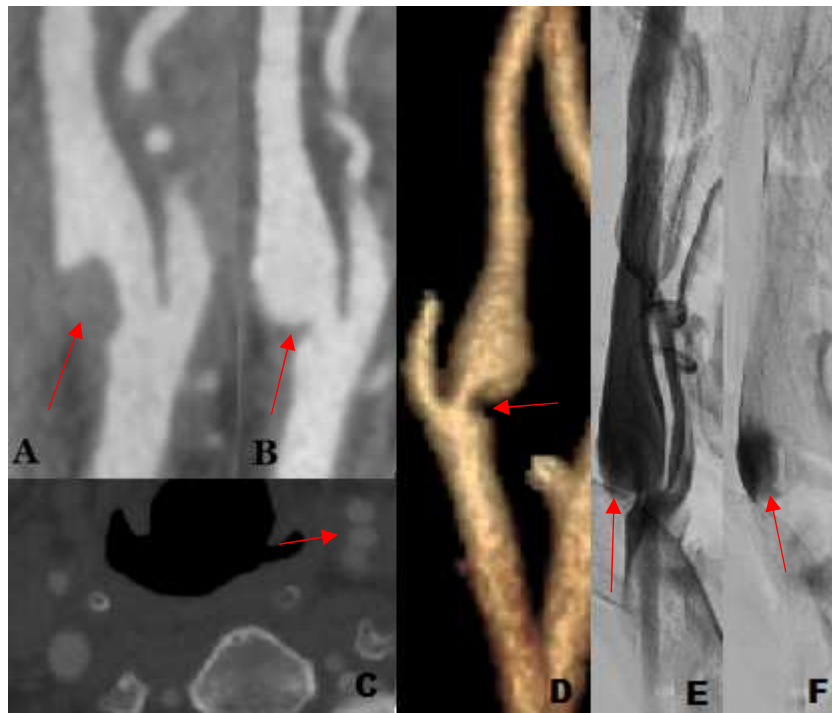


Figure 2



Parameter (n=266)	iCaW (n = 21)		Absence of iCaW (n = 245)		P
Mean age in years ± SD	50.6	(±9.2)	50.4	(±10.7)	0.76*
Sex (Female)	11/21	52.4%	101/245	41.2%	0.32 [†]
Active Smoking (250)	9/21	42.9%	112/229	48.9%	0.65 [†]
Absence of vascular risk-factors (261)	8/21	38.1%	58/240	23.7%	0.19 [†]
Stroke history	1/21	4.8%	37/245	15.1%	0.49 [†]
General vascular history (Coronary or peripheral arterial disease or angioplasty)	0/21	0%	21/245	8.6%	0.33 [†]
Dyslipidemia (256)	2/21	9.5%	37/235	15.7%	0.75 [†]
Hypertension (264)	8/21	38.1%	74/243	30.4%	0.47 [†]
Diabetes (259)	2/21	9.5%	33/238	13.9%	0.75 [‡]
Patent foramen ovale	3/21	14.3%	66/245	26.9%	0.30 [†]
Initial NIHSS (261) Median (IQR)	2.0 (0.0;6.0)		2.0 (0.0;6.0)		0.46*
Intracranial Proximal occlusion (263) (carotid, M1 or M2 proximal)	13/21	61.9%	91/242	37.6%	0.03 [‡]
Antithrombotic therapy before IS (208)					
- None	20/21	95.2%	158/187	84.5%	0.45 [†]
- Antiplatelet	1/21	4.8%	27/187	14.4%	
- Anticoagulant	0/21	0%	2/187	1.1%	

Table 1

*for Wilcoxon-Mann-Whitney test; [†] for Fischer test; [‡] for chi2 test; NIHSS: National Institute of Health Stroke Score; IS: Ischemic Stroke; IQR: Interquartile range.

Sex	Age	Ethnics	Initial NIHSS	Bilateral CaW	CaW Length (mm)	CaW stenosis NASCET (%)	Proximal occlusion (M1 or M2)	Ipsilateral Stroke Recurrence (months)	CaW stenting (months)	Time Delay without recurrence (month)	Superimposed thrombus
F	63	Caucasian	16	No	1.6	0	Yes	No	No	55	No
M	53	Caucasian/African	0	Yes	2.0	0	No	31	34	N/A	Yes
M	43	Middle eastern	3	No	6	0	No	Lost to follow up	N/A	N/A	No
M	62	Asian	3	No	3.3	0	Yes	0,5 and 1	45	N/A	Yes
M	50	Caucasian	12	No	2.6	0	Yes	No	No	44	No
M	40	Caucasian	10	Yes	5.2	50	Yes	No	1	36	Yes
F	55	Caucasian	1	No	2.9	0	No	No	No	33	No
F	61	Caucasian	2	No	3.6	0	No	No	17	27	No
M	46	Caucasian	25	No	2.5	0	Yes	No	19	28	No
F	48	Caucasian	2	No	2.4	0	No	No	No	24	Yes
F	49	Middle eastern	0	No	1.8	30	Yes	0,03	2	N/A	No
M	60	Caucasian	15	No	3,1	2	Yes	No	1	8	No

M	49	Caucasian	0	No	3,8	38	No	No	1	21	No
F	33	Caucasian	0	No	3	16	No	No	0,5	13	Yes
M	64	Middle Eastern	17	No	3,2	2	Yes	No	1	10	No
F	35	Caucasian	4	No	3	0	Yes	No	2	NA	No
F	60	Caucasian	2	No	3,1	0	Yes	No	No	22	No
F	41	Caucasian	0	No	4,6	5	Yes	6.8	8	27	No
M	42	Caucasian	12	No	NM	NM	Yes	No	0	20	Yes
F	49	Caucasian	0	Yes	3,4	0	No	No	2	4	No
F	56	Caucasian	1	Yes	2,1	0	No	No	No	7	No

Table 2

Appendix:

Every CTA was performed on a 64-row multidetector scanner with 128 slices per rotation, with acquisitions ranging from under the aortic arch to the Willis circle. The following scanning parameters were used: slice thickness 0.625 mm; gantry rotation time 0.5 seconds; pitch 0.516:1; voltage 120 kV; current maximum 350mA with Automatic Exposure Control. 70 mL of intravenous contrast agent (Xenetix 350, 100mL of Iobitridol, 350mg/mL, Guerbet, Villepinte, France) were injected with a 40mL saline flush by an automated contrast injector. Images were reconstructed using axial, coronal, sagittal and 3D volume reconstructions.