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Carotid artery atherosclerosis is not associated with hyoid proximity: Results from a cross-sectional and longitudinal cohort study

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ABSTRACT

Introduction: Cervical internal carotid artery (ICA) atherosclerotic plaque and stenosis is often asymmetric. We hypothesized that hyoid bone proximity to the ICA also may be asymmetric and may increase the risk of traumatic endothelial injury and accelerate atherosclerotic stenosis.
Methods: A retrospective cross-sectional and longitudinal cohort design evaluated consecutive adult patients at 3 hospitals who underwent repeat computed tomography angiography (CTA) of the neck 2 calendar years apart (01/2000–07/2017). ICA plaque thickness, luminal stenosis, and their progression over time were compared between side with the nearer hyoid wing (proximal side) to the further side (distal side).
Results: Sixty-six patients were included with a median age of 64y (IQR 53–73), 37 (56.1%) female, had a median hyoid-ICA distance of 3.06 mm (IQR 1.27–6.20 mm) and median difference between sides of 2.11 mm (IQR 0.70–3.97 mm). The median plaque thickness was 3.5 mm (IQR 2–4) and median stenosis was 10% (IQR 0–33%). Comparing the proximal to distal side, there was no difference in ICA plaque thickness (median 2.5 mm [IQR 1–4] vs. 3.0 mm [IQR 2–4], $p = 0.366$) or stenosis (7% [IQR 0–31%] vs. 12% [IQR 0–39%], $p = 0.21$). After a median follow-up of 1002 days (range 392–3397 days), there was no difference in the change in plaque thickness (0.5 cm [IQR 0–1] vs. 0.0 cm [IQR −0.5–0.5], $p = 0.21$) or stenosis (0% [IQR −2.5–13%] vs. 0% [IQR −6–5%], $p = 0.34$) between proximal and distal ICAs.
Conclusions: The presence and progression of atherosclerotic plaque and stenosis were unrelated to hyoid-ICA distance in this cross-sectional and longitudinal cohort study.

1. Introduction

Carotid atherosclerotic stenosis is largely attributed to traditional cardiovascular risk factors such as hypertension, tobacco use, dyslipidemia, and diabetes, as well as non-modifiable risk factors including male sex and older age [1–4]. However, data from the Northern Manhattan Study indicates that these traditional risk factors may only account for 20% of total carotid plaque burden [5]. Furthermore, the fact that carotid atherosclerotic stenosis may develop in an asymmetric pattern is only partially understood [6]. Stenosis of the cervical carotid arteries typically occurs within the first two centimeters of the bifurcation. Plaque formation at this location has traditionally been attributed to turbulent flow and increased shear stress [7,8] which may be influenced by the angle at which the internal carotid artery (ICA) branches off the common carotid artery (CCA) [9]. However, the greater hyoid wing also lies within close proximity to the bifurcation of the CCA. The proximity of the ICA to the greater hyoid wing has been associated with an increased risk of ICA dissection [10], as well as endothelial dysfunction with resultant atherosclerosis, according to several small case series [11,12]. This remains unproven in larger comparative studies. In this investigation, we tested the hypothesis that internal carotid atherosclerotic plaque thickness, luminal stenosis, and their progression over time would be inversely related to the distance between the hyoid wing and the ICA.

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2. Materials and methods

2.1. Patient selection

We conducted a retrospective cohort study of adult patients over 18 years of age who underwent computed tomography angiography (CTA) of the neck on at least two occasions separated by at least two years' time (January 1, 2000–July 1, 2017) at any of 3 hospitals within our health system. Potentially eligible patients were excluded if radiology reports documented any of the following historical elements prior to the patient's first CTA: carotid occlusion, carotid dissection, history of neck surgery, carotid endarterectomy or stenting, radiation to the neck, vasculitis, or non-atherosclerotic vasculopathy (e.g., fibromuscular dysplasia) involving the carotid system. All patients who met inclusion criteria for the cross-sectional study were re-screened for inclusion in the longitudinal cohort study and were excluded from the longitudinal cohort study if he or she experienced a carotid occlusion or dissection, underwent neck surgery, carotid endarterectomy or stenting prior to any repeat CTA, had neck radiation, or were diagnosed with new vasculitis or non-atherosclerotic vasculopathy between interval CTAs.

2.2. Data abstraction

Patient-level and neuroimaging data elements were abstracted from the medical record and CTA source images, and were recorded using a secure, online data collection tool [13]. Patient demographic information, past medical history, and active medications were abstracted from the electronic medical record by a reviewer who was blinded to CTA findings.

2.3. Imaging

Imaging protocols were similar across study sites. At each site, unenhanced head CT was acquired using a third- or fourth-generation CT scanner with 5-mm thickness for the entire examination. Conventional brain window images were used. CTA images of the head and neck were acquired following the unenhanced CT using iodinated contrast (100 mL Isovue-370), administered intravenously through a 20-gauge (or larger) right antecubital intravenous catheter, when possible.

Two vascular neurology fellows (GK, CR) independently measured the distance between the greater hyoid wing and the ICA at the level of the carotid bifurcation. For this measurement, CTA source images were viewed in the axial plane. Each reader was instructed to make measurements of the shortest hyoid-ICA distance within 1 cm rostral or caudal to the carotid bifurcation, but not beyond this window. The shortest distance between each of the greater hyoid wings and the corresponding cervical ICA was determined.

Two neuroradiology fellows (AM, DG) independently measured ICA plaque thickness, ICA angles, ICA plaque features, and they quantified the degree of stenosis for each cervical ICA using NASCET criteria (Fig. 1) [14]. The ICA angle was calculated as the angle of deviation of the ICA from the rostral-caudal line drawn through the center of the CCA, as previously described [9]. While complete blinding of the interpreting physicians was not possible, the four readers were not informed of the hypothesis of the investigation. Additionally, raters measuring hyoid-ICA distance were blinded to the measured ICA plaque thickness, degree of stenosis, ICA angle, the side of any cerebral infarction (if present), and the formal radiology report. The raters of ICA plaque thickness, stenosis, and angle were blinded to final ICA-hyoid distance measurements, the side of any cerebral infarction (if present), and the formal radiology report. Each reader was requested not to perform any additional measurements. Acceptability of image quality was determined at the discretion of each reader prior to measurement acquisition (See Supplement).

2.3.1. Cross-sectional study

The prespecified primary outcome for the cross-sectional study was the thickness of ICA plaque. Secondary outcomes included the degree of ICA stenosis using NASCET criteria, the presence of any plaque, ulcerated plaque, and calcified plaque thickness [14]. These plaque features were compared between paired ICAs (proximal side vs. distal side), and were adjusted for ICA angle using linear or logistic regression, where appropriate.

A post-hoc sensitivity analysis was also performed, comparing ICA plaque thickness and the degree of stenosis between the 1st and 4th quartiles of hyoid-ICA distance using linear regression. These regression models were clustered by patient and adjusted for age, sex, ICA angle, and history of hypertension, diabetes, and dyslipidemia.

2.3.2. Longitudinal cohort study

The pre-specified primary outcome for the longitudinal cohort study was the change in plaque thickness from baseline to follow up imaging, while change in ICA stenosis from baseline to follow-up was a secondary outcome. These features were compared between the paired arteries (proximal side vs. distal side) with and without adjustment for ICA angle and delay to repeat CTA. In addition, we compared the change in plaque thickness and stenosis between the 1st and 4th quartiles of hyoid-ICA distance, clustered by patient, and adjusted for delay between CTA scans, age, sex, ICA angle, and history of hypertension, diabetes, and dyslipidemia.

2.3.3. Statistical analysis

Inter-rater agreement of each continuous measurement was calculated using the Pearson correlation coefficient while agreement between categorical measurements was assessed using Krippendorf's alpha [15], given the possibility of missing values due to poor image quality. Mean values for each continuous variable were calculated between the raters and used for analyses. In the event of excessively disparate measurements between readers (defined a priori as a difference in ICA stenosis > 30%, difference in ICA angle measurement by > 20°, or difference in hyoid-ICA measurement of > 5 mm), a third reader (JS) repeated the measurement, and this measurement was used in the analyses. In classifying categorical variables (e.g., presence of ulcerated plaque), such abnormalities were only counted if they were identified by *both* readers in order to optimize specificity of findings.

Categorical data were presented as percentages and compared using Chi-square or Fisher's exact test, where appropriate. Paired categorical data were compared using McNemar's test. Normality of data was determined using the Shapiro-Wilk test. Non-normally distributed continuous data were reported as medians with interquartile ranges and compared using the Wilcoxon Rank Sum test. The Wilcoxon signed-rank test was used to compare paired continuous variables. All tests were performed at the two-sided level using STATA 13.0 (College Station, TX), and p-values < 0.05 were considered statistically significant.

The relationship between ICA plaque thickness and hyoid-ICA distance was directly compared within each patient. The side with the shorter hyoid-ICA distance ("proximal side") was compared against the side with the greater hyoid-ICA distance ("distal side"). ICAs were also evaluated as independent events and grouped by hyoid-ICA distance quartile. To maximize sensitivity of detecting a difference, we compared ICA plaque and stenosis between the first and fourth hyoid-ICA distance quartiles.

This study was approved by the local Institutional Review Board. Data will be made available by the corresponding author upon request.

3. Results

3.1. Patient population and inter-rater reliability

Among 11,278 patients with CTA of the neck performed from 1/1/2000 to 07/31/2017, 656 patients had > 1 CTA neck available in our

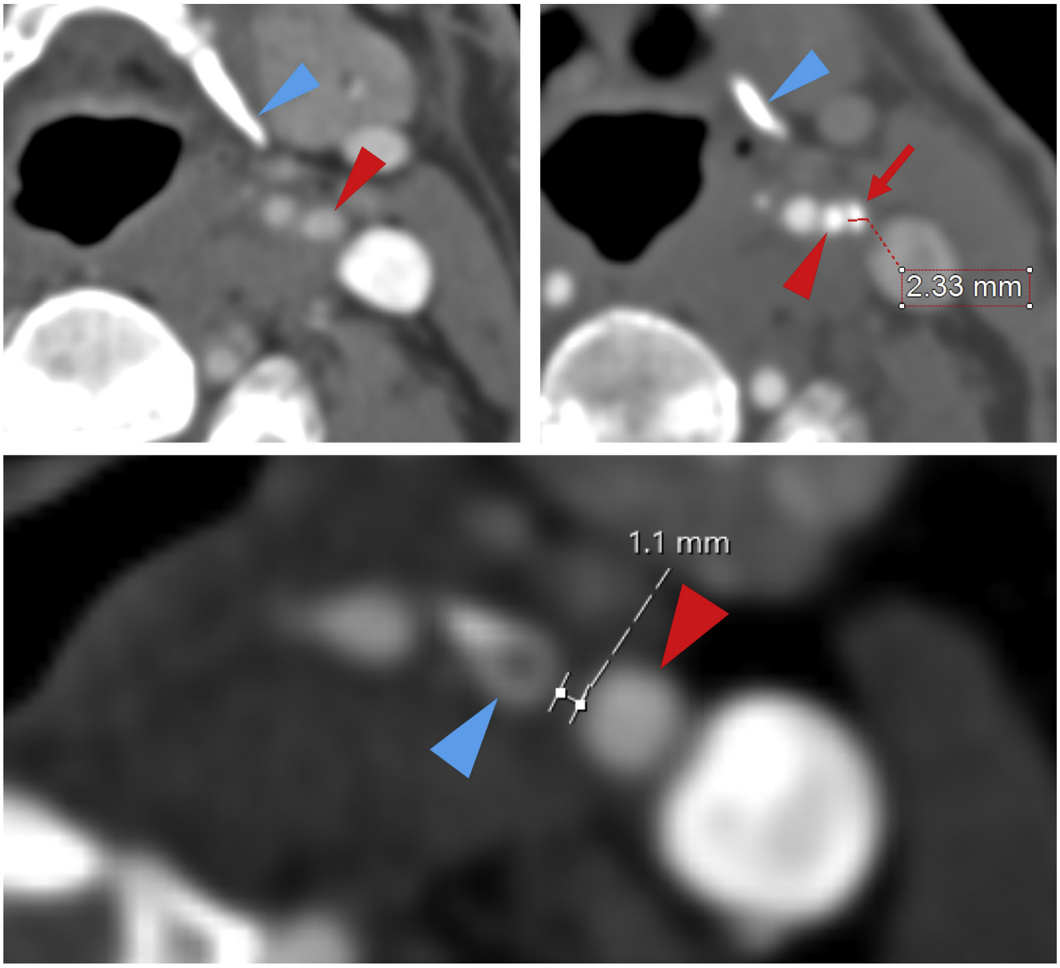

Fig. 1. Representative image.
Top left: Axial section of one patient's CTA with the greater wing of the hyoid identified (blue arrowhead) and no visible plaque in the left internal carotid artery (red arrowhead). Top right: Follow-up CTA 6 years later identifying new 2.33 mm calcified plaque (red arrow) affecting the previously normal left internal carotid artery. Bottom: Shortest distance between the greater hyoid wing (blue arrowhead) and the left internal carotid artery (red arrowhead) was measured at 1.1 mm.
CTA denotes computed tomography angiography. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 1
Demographics by study design

	Cross-sectional study (n = 66)	Cohort study (n = 46)
Age, median y (IQR)	64 (53–73)	63.5 (50–74)
Sex, no. female	37 (56.1%)	24 (52.2%)
Race, no. (%)		
Caucasian	38 (57.6%)	26 (56.5%)
Black	22 (33.3%)	17 (40.0%)
Other	6 (9.1%)	3 (6.5%)
Past medical history, no. (%)		
Hypertension	47 (71.2%)	34 (73.9%)
Diabetes mellitus	13 (19.7%)	7 (15.2%)
Dyslipidemia	41 (62.1%)	27 (58.7%)
Coronary artery disease	15 (22.7%)	12 (26.1%)
Peripheral vascular disease	4 (6.1%)	3 (6.5%)
Any prior tobacco use	30 (45.5%)	18 (39.1%)
Pack-year tobacco use, median (IQR)	21.5 (12–42.5)	16.5 (15–40)
Medications, no. (%)		
Statin	33 (50.0%)	22 (47.8%)
Fibrate	2 (3.0%)	1 (2.2%)
Other lipid-lowering therapy	7 (10.6%)	5 (10.9%)
Aspirin	28 (42.4%)	15 (32.6%)
Anti-hypertensive agent	37 (56.1%)	26 (56.5%)
Insulin	2 (3.0%)	0 (0.0%)

IQR denotes interquartile range.

electronic medical records, 66 of whom had repeat scans ≥2 calendar years apart and were included in the cross-sectional study. The median age of patients in the cross-sectional study was 64 years (IQR 53–73), 37 (56.1%) were female, and 28 (42.4%) were non-White (Table 1). The majority of initial CTAs were ordered due to stroke or transient ischemic attack (63.6%), while carotid disease identified on another imaging modality (12.1%) and head or neck injury (6.1%) were the next most common reasons identified. There was a strong inter-rater agreement for ICA stenosis (r = 0.856), hyoid-ICA distances (r = 0.842), and substantial agreement on plaque thickness (r = 0.608) and the presence of ICA plaque (α = 0.619; Supplementary Table 1). Plaque thickness and degree of ICA stenosis strongly correlated across the cohort (r = 0.727).

3.2. Cross-sectional study outcomes

Of the 66 included patients in the cross-sectional study (132 paired ICAs), the median hyoid-ICA distance was 3.06 mm (IQR 1.27–6.20 mm), with a median difference in hyoid-ICA distances between paired vessels of 2.11 mm (IQR 0.70–3.97 mm). The median plaque thickness was 3.5 mm (IQR 2–4 mm), and the median stenosis was 10% (IQR 0–33%).

There was no difference in the thickness of ICA plaque when compared between the proximal and distal sides (Table 2), and this

Table 2
Relationship between hyoid-ICA distance and selected outcomes in the cross-sectional study

	Proximal ICA[a] (n = 66)	Distal ICA[a] (n = 66)	p-Value	Adjusted[b] odds ratio/regression coefficient	95%CI	p-Value
Primary outcome						
ICA plaque thickness, median mm (IQR)	2.5 (1–4)	3 (2–4)	0.366	0.005[c]	−0.52–0.53	0.986
Secondary outcomes						
Any ICA plaque, no. (%)	36 (55%)	45 (68%)	0.020	0.47	−0.21–1.04	0.063
Calcified ICA plaque, no. (%)	17 (26%)	15 (23%)	0.724	0.61	0.31–1.23	0.167
Calcified plaque thickness, median mm (IQR)	1 (0–2.5)	1.5 (0–2.5)	0.318	0.02[c]	−0.45–0.50	0.922
Ulcerated ICA plaque, no. (%)	6 (9%)	6 (9%)	1.000	1.01	0.30–3.39	0.992
ICA stenosis, median % (IQR)	7% (0–31%)	12% (0–39%)	0.210	−2.25[c]	−11.18–6.68	0.619

ICA denotes internal carotid artery, CI confidence interval, and IQR interquartile range.
[a] Proximal ICA refers to the internal carotid artery for a given patient that is most proximal to the greater hyoid wing, whereas the distal ICA refers to the contralateral internal carotid artery, which is relatively more distal to that side's greater hyoid wing.
[b] Odds ratio and regression coefficients were adjusted for internal carotid artery angle.
[c] Regression coefficient.

remained non-significant after adjustment for ICA angle in linear regression (adjusted β = 0.005, 95%CI −0.52–0.53, p = 0.986). The presence of any plaque was more common on the side further from the hyoid wing compared to the closer side (68% vs. 55%, p = 0.020), and this trended toward significance after adjustment for ICA angle (adjusted OR 0.47, 95%CI −0.21–1.04, p = 0.063). There were no other differences in the degree of ICA stenosis, presence of calcified plaque, thickness of calcified plaque, or the presence of ulceration between the two sides, before or after adjustment for ICA angle (Table 2).

ICA plaque thickness was no different between ICAs in the 1st versus 4th hyoid-ICA distance quartiles (unadjusted β = −0.09, 95%CI −0.92–0.75, p = 0.839; Fig. 2A). This relationship remained unchanged after adjusting for age, sex, ICA angle, and history of hypertension, diabetes, and dyslipidemia (β = −0.67, 95%CI −2.05–0.71, p = 0.325). Similarly, there was no significant increase in the degree of stenosis for ICAs in the first versus fourth hyoid-ICA distance quartile (unadjusted β = 11.64, 95%CI −2.19–25.48, p = 0.097; Fig. 3A). After adjustment for age, sex, ICA angle, delay to CTA, and history of hypertension, diabetes, and dyslipidemia, this relationship remained nonsignificant (β = 2.28, 95%CI −13.93–18.48, p = 0.776).

3.3. Longitudinal cohort study outcomes

Of the 66 patients from the cross-sectional study, 14 (21.2%) were excluded after having undergone interval carotid endarterectomy or stenting before the follow-up CTA, 1 (1.5%) for neck surgery other than endarterectomy, 1 (1.5%) for a new carotid occlusion, 1 (1.5%) for neck radiation, and 3 (4.5%) due to incomplete follow-up CTA source images. Of the 14 patients who underwent stenting or endarterectomy at follow-up, 8 (57%) underwent revascularization on the side more proximal to the hyoid wing versus 6 (43%) with intervention to the opposite side (p = 0.290). The remaining 46 patients (92 paired ICAs) were included in the longitudinal cohort study. A total of 150 patient-years (54,771 patient-days) of data was available for final analysis, with a median of 1002 days (range 392–3397 days) between CTAs for each included patient.

Change in plaque thickness was no greater among ICAs that were more proximal to the hyoid wing (unadjusted β = −0.06, 95%CI −0.21–0.33, p = 0.659; Table 3). There remained no increase in plaque thickness for proximal ICAs after adjustment for ICA angle and delay to CTA (β = 0.01, 95%CI −0.28–0.31, p = 0.933), or when comparing between 1st and 4th hyoid-ICA distance quartiles (unadjusted β = −0.21, 95%CI −0.91–0.48, p = 0.531). After adjustment for age, sex, ICA angle, delay to CTA, and history of hypertension, diabetes, and dyslipidemia, there remained no increase in plaque thickness among ICAs in the first versus fourth hyoid-ICA distance quartiles (*β = −0.04, 95%CI −0.82–0.74, p = 0.915*).

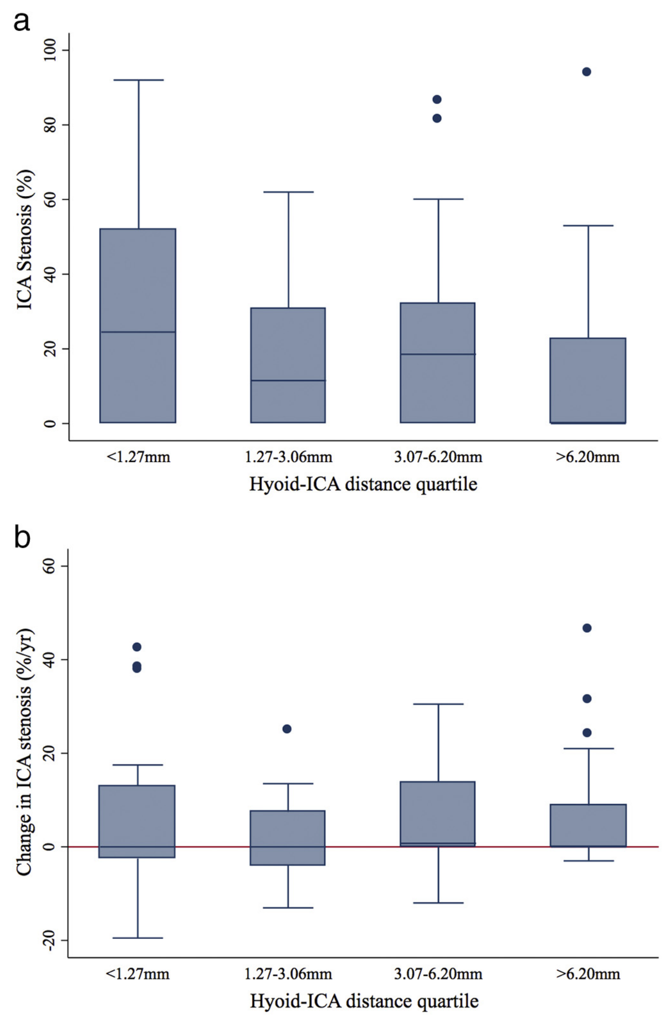

Fig. 2. ICA plaque thickness by distance from the greater hyoid wing.
A) Median cervical ICA plaque thickness (in mm) with interquartile range, grouped by hyoid-ICA distance quartile among patients in the cross-sectional study. B) Median change in cervical ICA plaque thickness (in mm/yr between interval imaging studies) with interquartile range, grouped by hyoid-ICA distance quartile among patients in the longitudinal cohort study.
ICA denotes internal carotid artery.

There were generally modest changes in the degree of stenosis over time, and no difference in these changes based on proximity of the hyoid wing (unadjusted β = −0.49, 95%CI −4.39–3.40, p = 0.799).

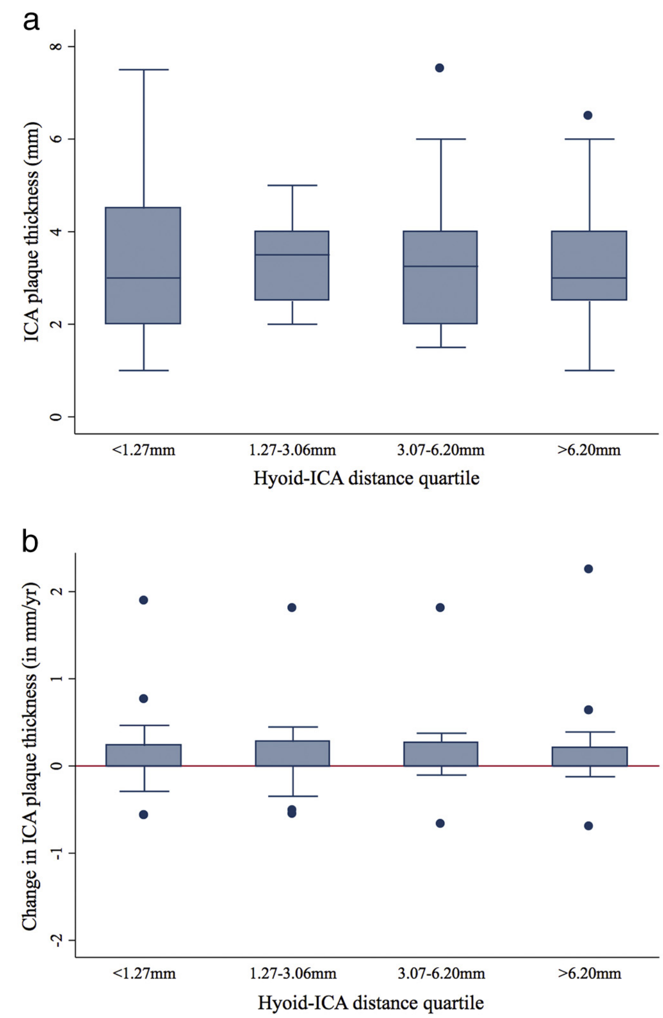

Fig. 3. ICA stenosis by distance from the hyoid wing.
A) Median cervical ICA stenosis (according to North American Symptomatic Carotid Endarterectomy Trial criteria) with interquartile range, grouped by hyoid-ICA distance quartile among patients in the cross-sectional study. B) Median change in cervical ICA stenosis (in percent/yr between interval imaging studies) with interquartile range, grouped by hyoid-ICA distance quartile among patients in the longitudinal cohort study.
ICA denotes internal carotid artery.

After adjustment for ICA angle and delay to CTA, there remained no significant change in ICA stenosis ($\beta = -0.37$, 95%CI -4.13–3.38, $p = 0.842$) comparing proximal ICAs versus distal ICAs. Further, comparing the 1st vs 4th quartile hyoid-ICA distance, there was no difference in increase in stenosis (unadjusted *$\beta = -1.48$, 95%CI -12.04–9.09, $p = 0.777$;* Fig. 3B). After adjustment for age, sex, ICA angle, delay to CTA, and history of hypertension, diabetes, and dyslipidemia, there remained no significant increase in stenosis over time (*$\beta = -1.01$, 95%CI -15.26–13.23, $p = 0.885$)* among ICAs in the 1st versus 4th distance quartiles.

4. Discussion

In this cross-sectional and longitudinal cohort study, we observed no increased risk of atherosclerotic plaque or stenosis for ICAs associated with shorter hyoid-ICA distances. While several case reports have suggested that asymmetric carotid plaque may be attributed to the proximity of the hyoid wing, it is unlikely that this relationship explains the development of atherosclerotic plaque or stenosis for most patients. We did observe a weak inverse association between hyoid-ICA proximity and presence of any plaque ($p = 0.063$) indicating a higher probability of plaque among more *distal* carotids. Given that there is no biologically plausible basis for this finding, and no other comparison showed a significant effect in this direction, we believe this difference in plaque to be a chance finding.

Major risk factors for the development of ICA atherosclerosis have been well characterized and include hypertension, diabetes, dyslipidemia, and tobacco use [16]. However, these systemic factors may only account for 20–50% of the asymmetric plaque burden observed in patients with carotid atherosclerotic disease [4,5]. Non-traditional vascular risk factors such as the ICA/CCA ratio [17], the ratio of outflow to inflow area [18], the ICA angle [9], and other structural factors [6,19,20] are also thought to contribute to plaque formation and progression. Unlike systemic factors, these and other physical traits may explain the asymmetry that is observed in patients with carotid atherosclerosis.

ICA geometry and tortuosity have been extensively studied and correlate with asymmetric plaque formation. In one of the earliest investigations on the relationship between ICA geometry and carotid disease, Sitzer and colleagues used high-resolution ultrasonography to correlate carotid plaque burden with carotid tortuosity [21]. Specifically, the investigators measured the angle made by the ICA and external carotid artery as they relate to the CCA when viewed in the *axial* plane. From this retrospective analysis of 1300 patients, the authors found that a wider angle strongly correlated with ipsilateral plaque formation at the ICA bulb, but had no relationship with age, sex, or traditional vascular risk factors [21]. In a separate study, Phan and colleagues also examined the relationship between ICA bifurcation tortuosity and plaque formation [9]. Using a novel approach, the investigators calculated the *vertical* angle of ICA trajectory as it branches from the CCA. With each increasing degree of the ICA angle, according to this report, the odds of ≥30% ICA stenosis grew by 5% (OR 1.05, 95%CI 1.04–1.07). The investigators from each of these studies concluded that suboptimal geometry may contribute to abnormal hemodynamic forces, resulting in reduced shear stress and more turbulent flow, which ultimately lead to carotid arteriosclerosis and plaque formation. For this reason, we included ICA angle among our multivariable regression models assessing both the presence and progression of ICA atherosclerotic disease.

In addition to disturbances of laminar flow, a number of case reports have suggested that hyoid wing proximity has also been associated with atherogenesis and cerebral ischemia [11,12,22–24] –findings which prompted the present investigation. For example, Abdelaziz et al.

Table 3
Changing ICA features over time comparing the side closest to the hyoid wing to the farther side

	Proximal ICA[a] (*n* = 46)	Distal ICA[a] (n = 46)	*p*-Value	Adjusted[b] regression coefficient	95%CI	*p*-Value
Change in ICA plaque thickness, median mm (IQR)	0.5 (0–1)	0 (−0.5–0.5)	0.209	0.01	−0.28–0.31	0.933
Change in ICA stenosis, median % (IQR)	0% (−2.5–13%)	0% (−6–5%)	0.337	−0.37	−4.13–3.38	0.842

ICA denotes internal carotid artery and IQR interquartile range.
[a] Proximal ICA refers to the internal carotid artery for a given patient that is most proximal to the greater hyoid wing, whereas the distal ICA refers to the contralateral internal carotid artery, which is relatively more distal to that side's greater hyoid wing.
[b] The regression coefficient was clustered by patient and adjusted for delay to repeat imaging and ICA angle.

described an 85-year-old woman with symptomatic (90%) stenosis of the right ICA with indentation of the hyoid wing at the level of plaque. Similar findings were reported in later case reports where significant ICA plaque or thrombus were found in close proximity to the greater hyoid wing [11,24], including one case [23] which provided videographic evidence for recurrent ICA compression by the greater hyoid wing with routine head turning and swallowing. A separate case report of one young male without any vascular risk factors or relevant family history provided histopathologic evidence for plaque formation in an ICA that directly abutted the hyoid wing and resulted in recurrent cerebrovascular ischemia [25]. In each of these case reports, the authors concluded that microtraumatic forces accelerated plaque formation and increased the risk of artery-to-artery embolism. In another report of a patient with transient ischemic symptoms, the authors attributed the patient's recurrent focal deficits to a proximal hyoid wing in the absence of atherosclerosis [26]. In this case, the elongated hyoid wing was hypothesized to intermittently compress the ICA, resulting in transient ischemic attack. Hyoid wing resection in each of these cases has been associated with favorable neurologic outcomes and prevention of further ischemic events [12,25–27].

In spite of these individual case reports, our findings suggest that there is likely no clinically meaningful relationship between hyoid proximity and the development of ICA atherosclerosis for the majority of patients.

This study was limited by its relatively small sample size due to the pre-specified decision to include a longitudinal comparison (two CTA studies, at least two calendar years apart) to look at plaque and stenosis progression. As plaque accumulates in the carotid artery, the vessel enlarges, which could be a major confounder when evaluating the distance to the hyoid bone. Thus, we felt it was important to include a longitudinal component to this study to ensure that hyoid-ICA proximity led to atherosclerosis and not the converse. Together, the cross-sectional study permitted prevalence estimates and could have illustrated an association while the longitudinal cohort study could have strengthened the argument for causation. We also selectively investigated the anatomic relationship between the hyoid wing and the cervical ICA, and not any other adjacent structures. Numerous reports have documented the association between styloid length and carotid dissection [10,28], however any potential association between styloid length and carotid atherogenesis remains unproven.

By selecting patients for the longitudinal cohort study based on the availability of repeat neck imaging, it is possible our data overestimates the risk of progression in carotid atherosclerosis due to selection bias. Patients requiring additional imaging may have been at greatest risk for progressive stenosis. Conversely, by excluding patients who underwent carotid intervention (n = 14/66) before the follow-up CTA, we may be underestimating the risk of progressive atherosclerosis or the development of symptomatic disease (time-window bias). Importantly, endarterectomy or stenting were performed with similar probability on the side with a proximal hyoid wing (57%) versus distal hyoid wing (43%). Such biases would be reduced with a prospective observational cohort of asymptomatic patients.

Finally, our study predominantly captured data on patients with mild cervical carotid disease. While the majority of included patients had some degree of cervical ICA plaque, and many had comorbid vascular risk factors or were imaged for stroke, most patients had no hemodynamically significant stenosis. A study limited to patients with significant ICA atherosclerotic stenosis, where plaque progression or rupture may be accelerated by hyoid proximity, may be more sensitive to detect an association.

5. Conclusions

In this cross-sectional and longitudinal retrospective cohort study, we found no significant increase in the risk of atherosclerotic plaque thickness or luminal stenosis among ICAs closer to the greater hyoid wing. Additional studies are needed to explain the mechanisms by which plaque develops asymmetrically in cervical carotid vessels.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinimag.2019.05.016.

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