Geometric Factors of the Bifurcation in Carotid Atherogenesis

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In vitro studies have demonstrated that geometry of the carotid bifurcation predicts blood flow alterations associated with atherosclerotic plaque formation. We investigated intraindividual asymmetry of carotid atherosclerosis by measuring geometric aspects of the carotid bifurcation. We measured diameter stenosis, the internal carotid artery/common carotid artery area ratio, and the angle of the carotid bifurcation on 40 arteriograms. Stenosis asymmetry was significantly associated with area ratio asymmetry \((r=0.355, p<0.025)\); there was no such association between stenosis asymmetry and bifurcation angle asymmetry. Geometric factors of the carotid bifurcation, particularly the area ratio, may help explain intraindividual asymmetry in carotid atherosclerosis. (Stroke 1990;21:267-271)

Carotid artery atherosclerosis develops at the common carotid bifurcation, particularly the carotid sinus. One puzzling aspect of carotid atherogenesis is asymmetry of the bifurcation lesions. Since the bifurcations of a given individual are exposed to identical risk factors such as hypertension, diabetes, and hyperlipidemia, one might expect bifurcation lesions to be similar for both carotid arteries. While the risk factor exposure of each bifurcation should be similar for each individual, the bifurcations themselves could have substantial left-right asymmetry. Geometric aspects of the bifurcation (e.g., the ratio of the areas of daughter to parent arteries, and the angle of the bifurcation) are important in the development of flow disturbances in scale models of arterial bifurcations. The purpose of our investigation was to evaluate these geometric features of the bifurcation in the context of asymmetry of carotid atherosclerosis. Specifically, we hypothesized that increasing asymmetry of carotid atherosclerosis was associated with increasing asymmetry of bifurcation geometry.

**Subjects and Methods**

We examined all available conventional, nonmagnified, bilateral, selective carotid arteriograms performed between 1980 and 1987 at the Hospital of the Good Samaritan, Los Angeles, California. We included in the study good-quality arteriograms performed on men aged ≥50 years. We excluded arteriograms if 1) both bifurcations were normal, 2) carotid endarterectomy had been performed previously, 3) fibromuscular dysplasia or carotid dissection was present, or 4) maximal diameter stenosis occurred in the common carotid artery (CCA) or >2 cm distal to the carotid bifurcation.

We used calipers to measure lumen diameter to the nearest half millimeter on the lateral projection since vessel overlap in the anteroposterior view frequently obscured either the bifurcation angle or the point of maximal internal carotid artery (ICA) stenosis. We measured CCA diameter 2 cm proximal to the bifurcation; if the lumen was narrowed at this site, we made measurements just proximal to such a lesion. Similarly, we measured ICA diameter 2 cm distal to the bifurcation; if the lumen was narrowed at this site, then we made measurements immediately distal to such a lesion. Diameter stenosis was defined as the largest percent narrowing of the diameter of the proximal ICA. We defined the ICA/CCA area ratio as the cross-sectional area of the ICA divided by that of the CCA. The bifurcation angle was measured as follows: the arteriographic outline of the outer walls of the ICA and the external carotid artery on the lateral view were extended proximally (toward the CCA) until both lines met; the angle at this junction was considered the bifurcation angle.

Due to the presence of plaque at the ICA origin, we were not consistently able to measure a nonstenotic ICA origin and instead used the ICA diameter measured 2 cm distal to the bifurcation. We compared the ICA/CCA area ratio used in this study with the area ratio used by Karino and Goldsmith (the sum of the cross-sectional areas measured at the...
Lesion asymmetry was defined as the difference (left minus right) in diameter stenosis for the ICA. Asymmetry of the ICA/CCA area ratio was defined as the difference (left minus right) between the two ratios divided by their mean for that individual, expressed as a percentage. Asymmetry of the bifurcation angle was defined as the difference (left minus right) between the two measured angles for an individual. Results are given as mean±SD. Statistical analysis was performed using simple linear correlation, with probabilities determined using one-tailed analysis.

Results

We reviewed 325 arteriograms; 40 met all criteria for study entry. The average age of the patients was 67.2 (range 53–83) years. We found ICA stenoses in 69 (86%) of the 80 arteries, with 63 of the 69 lesions maximal opposite the flow divider, and normal studies in the remaining 11 (14%) (mean±SD stenosis 27.0±23.2%, maximum 85.7%; Table 1). ICA/CCA area ratios averaged 0.75±0.13 (range 0.39–1.0). Bifurcation angles averaged 34.0±21.7° (range 2–111°). Diameter stenosis, ICA/CCA area ratio, and bifurcation angle for the left carotid arteries were 24.8±21.5%, 0.76±0.13, and 34.5±22.3°, respectively. For the right carotid arteries, these values were 29.3±24.8%, 0.73±0.14, and 33.6±21.3°, respectively.

Intrapatient asymmetries in diameter stenosis averaged 29.3±20.7% (range 0–76.5%); those in the ICA/CCA area ratio and bifurcation angle averaged 17.3±12.3% (range 0–60.1%) and 13.2±15.4° (range 0–65.5°), respectively. Stenosis asymmetry was significantly correlated with ICA/CCA area ratio asymmetry (r=0.355, p<0.025; Figure 2). When the 32 patients having at least one artery with <22% diameter stenosis (approximately 40% area stenosis) were eliminated from the analysis, the correlation between stenosis asymmetry and ICA/CCA area ratio asymmetry for the remaining eight patients was still significant (r=0.644, p<0.05). Significant correlation between diameter stenosis asymmetry and ICA/CCA area ratio asymmetry was also observed for 26 patients after the 14 patients having at least one artery with >50% diameter stenosis were eliminated from the analysis (r=0.547, p<0.0025; Figure 3). There was no significant association between diameter stenosis asymmetry and bifurcation angle asymmetry (r=0.016).

Our ICA/CCA area ratio was significantly associated with the area ratio used by Karino and Goldsmith4 (r=0.485, p<0.025; data not shown).

Discussion

We show that intrapatient asymmetry of the ICA, averaging 29% diameter stenosis, was significantly associated with asymmetry of the ICA/CCA area ratio of the carotid bifurcation (r=0.355). This association was stronger (r=0.547) when patients having at least one artery with >50% diameter stenosis were eliminated from the analysis. We suggest that this geometric feature may have a causal role in plaque formation, particularly early lesion development.

Studies of scale models of carotid bifurcations and postmortem arterial segments show that the normally axially aligned, unidirectional blood flow of the artery changes at the bifurcation; complex secondary flow patterns consisting of vortices (or recirculation zones) develop at the bifurcation opposite the flow divider.6,7 Unidirectional laminar flow, as seen on the side of the flow divider, is associated with relatively high shear stresses and sparing from intimal thickening and atherosclerotic plaque development. Atherosclerotic lesions tend to develop opposite the flow divider where low shear stresses, resulting in vortex formation, are found.6 This was also illustrated in our study, with 91% (63 of 69) of ICA lesions found opposite the flow divider. The consequences of vor-
vessel and lowest velocity at the periphery) results in bifurcation, the presence of a parabolic velocity distribution (i.e., highest velocity at the center of the region, when acted upon by a transverse pressure gradient occurring when the flow changes direction, develops secondary flow regions opposite the flow divider.

The geometry of a bifurcation is of substantial importance in determining the size of secondary flow regions, or vortices. Vortex size increases markedly following an increase of the area ratio defined as the sum of the cross-sectional areas of the daughter vessels divided by the cross-sectional area of the parent vessel. Increasing bifurcation angle is also associated with increasing vortex size, although this
effect is smaller than that of the area ratio. In addition, the radius of curvature of the outer wall at the bifurcation is associated with vortex size; a larger radius of curvature (i.e., a gentle bend) is associated with a smaller vortex. We found a significant association between diameter stenosis asymmetry and ICA/CCA area ratio asymmetry; bifurcation angle asymmetry was not associated with diameter stenosis asymmetry. Our findings are in good agreement with those of Karino and Goldsmith, who found that the bifurcation angle seems less important than the area ratio as a determinant of vortex size.

The association between diameter stenosis asymmetry and ICA/CCA area ratio asymmetry was stronger when patients having at least one artery with >50% diameter stenosis were eliminated from the analysis, suggesting that geometric factors are particularly important for early lesion development. In this study, stenosis may also have several confounding features. First, increasing diameter stenosis of the ICA results in a smaller ICA/CCA area ratio. Second, increasing diameter stenosis beyond 50% may begin to reduce blood flow in this region, resulting in altered flow rate ratios, which themselves affect vortex formation. It seems apparent that increasing stenosis adds substantial complexity to the determinants of vortex formation at the carotid bifurcation.

Our results appear to agree with those of Caplan and Baker, who demonstrated an association between size of the CCA and ICA occlusion or stenosis. They found that carotid occlusion tends to occur on the side of the smaller CCA and that smaller CCA tend to give rise to more stenotic ICA. One interpretation of these findings is that a smaller CCA means a larger ICA/CCA area ratio. A contrasting study is that of Harrison and Marshall, who found 1) no association between vessel size and the presence of atherosclerotic plaques and 2) a tendency for plaques to be found at bifurcations with larger ICA-CCA angles. It may be that the wide variety of risk factor exposures of different individuals may mask the significance of some geometric features of the bifurcation and that this significance can be best demonstrated when systemic risk factors are held constant. The latter situation is achieved when evaluating intraindividual asymmetry.

Several additional points of our study need to be addressed. First, the correlation coefficients, while significant, explain only a minority of the variability in diameter stenosis asymmetry. For example, a correlation coefficient of 0.355 explains only 12.6% of the variation. While this proportion of variability explained becomes larger (29.9%) if patients with at least one >50% stenotic vessel are removed from the analysis, it is clear that the majority of diameter stenosis asymmetries are not explained by ICA/CCA area ratio asymmetries. Limiting factors of our study include 1) arteriography, used for lumen measurements, does not measure plaque thickness and does not always distinguish normal vessel wall from atherosclerotic lesions. In addition, the radius of curvature at a bifurcation is difficult to assess using arteriography, and this potentially important variable was therefore not included in our study. 2) Our ICA/CCA area ratio is significantly associated with but not identical to the area ratio of Karino and Goldsmith.
Plaques at the origin of the ICA prevented us from regularly measuring nonstenotic lumen diameter in this region, which may be of particular importance for vortex formation because it is unaffected by poststenotic dilatation. 3) Our measurements could have been affected by minor patient rotation and by branches of the CCA not being in the plane of the parent artery. 4) We cannot rule out the possibility that increases in the ICA/CCA area ratio are secondary to increasing stenosis. Indeed, Glagov et al\textsuperscript{10} have reported that in the coronary artery system, compensatory enlargement of arteries occurs in the presence of increasing atherosclerosis until 40% area stenosis is present. To address the question of whether this phenomenon was present in our study, we repeated the data analysis excluding patients having at least one artery with <22% diameter stenosis (approximately 40% area stenosis). While only a small group remained (n=8), there was still a significant association between stenosis asymmetries and ICA/CCA area ratio asymmetries. This association is therefore not explained by the compensatory enlargement described in the coronary artery system.

Our findings are compatible with a model of carotid atherosclerosis in which carotid geometry, specifically the ICA/CCA area ratio plays a significant role in atherogenesis in this region. The significance of the ICA/CCA area ratio is most likely related to its impact on vortex size at the carotid bifurcation. This geometric feature may help explain left–right asymmetry of carotid atherosclerosis in a given patient.

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References

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