Response to Letter Regarding Article, “Patterns and Implications of Intracranial Arterial Remodeling in Stroke Patients”

We appreciate the opportunity to respond to comments by Gutierrez and Elkind1 about our recent article.2 We think that they misunderstood our imaging-based methodology and would like to offer reasons that might explain their discrepant results.3

The authors assert that plaque burden should be based on intimal area when determining the remodeling threshold. Our definition has been used in other published magnetic resonance imaging and intravascular ultrasound studies that demonstrate remodeling justifiably because atherosclerotic changes can extend beyond the internal elastic lamina. Furthermore, collinearity did not influence our results as suggested by Gutierrez and Elkind1 because we defined stenosis based on lumen reduction, unlike the definition used in pathological specimen studies.3,4 About the slope of the regression line, S is simply a variable that can be negative or positive depending on whether the vessel tapers or, uncommonly, enlarges from proximal to distal locations. Others have similarly used a variable to represent slope.5 Figure 1 is a schematic diagram to help conceptualize the use of this formula, and S would be negative to represent a tapering vessel. Gutierrez and Elkind1 are correct that the slope in supplemental Figure II should be negative and we appreciate bringing this to our attention.

In our article, we stated that “MRI measurements were obtained for all plaques detected in the proximal segments of the intracranial arteries” and then listed these segments (eg, M1, M2). Lesion site was defined as the location of the thickest wall for each segment and had nothing to do with a proximal location within a segment, as suggested by Gutierrez and Elkind.1 The reference site could be either proximal or distal to the plaque depending on where the wall was thinnest, as we explained in our article, and the sign of the slope changed accordingly. β coefficients were, therefore, appropriately positive or negative.

We disagree that selecting only symptomatic patients will bias results from increased wall thickness in neighboring intima. Imaging studies enable wall measurements of an entire vessel segment beyond the plaque site, unlike the specimen studies, Gutierrez and Elkind1 reference. Furthermore, most plaques included in our analysis were asymptomatic and not advanced high-grade lesions (Results section), despite our inclusion criteria.

About image resolution, we have previously shown that trained readers can make reasonably accurate visual interpolations of thin structures that overcome magnetic resonance imaging resolution limitations.6 Furthermore, we think that this constraint would favor against identifying outward remodeling because the increased outer wall area at the lesion site might be undetectable because of partial volume averaging from inadequate resolution.

As noted in our article, we were the first to report differences in remodeling between anterior and posterior circulations but not to report outward remodeling in brain arteries (references 18–21). Gutierrez et al1 reported no outward remodeling in brain arteries; however, they used a linear model to evaluate potentially nonlinear associations (remodeling). Importantly, one cannot identify a threshold for remodeling using a linear term in regression (no inflection point, Figure 2B3). In fact, the regression depicted in Figure 2B seems to show no significant change in lumen area with increasing stenosis, which supports remodeling. Furthermore, although a mixed model was used to adjust within-patient variation, adjustments for between-patient variation (eg, height, sex, and race) are also needed to enable comparability of data points. This would have a different effect than categorizing by size as was done in their study. The prediction of negative lumen areas (Figure 2D3) further highlights inappropriate use of this model. Consequently, we think that the article by Gutierrez et al3 does not disprove remodeling in brain arteries.

Disclosures

Drs Qiao and Wasserman have a patent pending (No. 13/922,111) for the black blood magnetic resonance imaging technique.

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