# Sex-differences in Carotid Plaque Composition in Patients with Embolic Stroke of Undetermined Source

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# Abstract

**Introduction**: Non-stenotic carotid plaque with high-risk vulnerable plaque features, such as intraplaque hemorrhage (IPH) and lipid-rich-necrotic-cores (LRNC), may be the cause of embolic ischemic stroke in some patients with embolic stroke of undetermined source (ESUS). Histologic studies of carotid endarterectomy specimens report differences in carotid plaque phenotypes by sex. We examined sex-differences in carotid plaque composition in patients with ESUS.

**Methods**: A retrospective cohort of patients with anterior circulation ischemic stroke imaged with neck CT angiography (CTA) who met criteria for ESUS or had atrial fibrillation (AF) were identified. Carotid artery bifurcations were analyzed with a semi-automated plaque quantification software. Plaque subcomponent (calcium, IPH, and LRNC) volumes were compared by sex.

**Results**: Ninety-four patients with ESUS (55% women) and 95 patients with AF (47% women) were identified. Women overall showed lower carotid calcium, IPH, and LRNC subcomponent volumes ipsilateral to the side of stroke in both ESUS and AF cohorts but volumetric sex-differences reached statistical significance only in the ESUS cohort for calcified plaque (19.6 vs 63.9 $mm^3$, $p<0.001$), and IPH (3.3 vs 9.4$mm^3$, $p=0.008$).

**Discussion**: Sex-differences in carotid plaque composition in ESUS suggest the possibility of a differential contribution of carotid atheroembolism as a source of stroke mechanism in men versus women.

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# Introduction

- In patients with embolic stroke of undetermined source (ESUS), a subset have atheroembolism from non-stenotic carotid plaque.
- An inflammatory plaque phenotype with vulnerable plaque components could suggest a higher likelihood of carotid atheroembolism.
- Histologic studies of carotid endarterectomy specimens suggest plaque composition in men more frequently show inflammatory plaque phenotypes compared to stable, fibrous phenotypes in women.
- We examined sex-differences in carotid plaque composition in an ESUS cohort to investigate whether men had higher volumes of vulnerable plaque components.

# Methods: Sample

- A retrospective observational cohort study was conducted at a single integrated hospital system at a comprehensive stroke center between October 1, 2015 to April 1, 2017.
- Patients 18 years or older with unilateral anterior circulation ischemic stroke and imaged with computed tomographic angiography (CTA) of the neck were included.
- Stroke etiology as atrial fibrillation (AF) versus ESUS was determined by a vascular neurologist.

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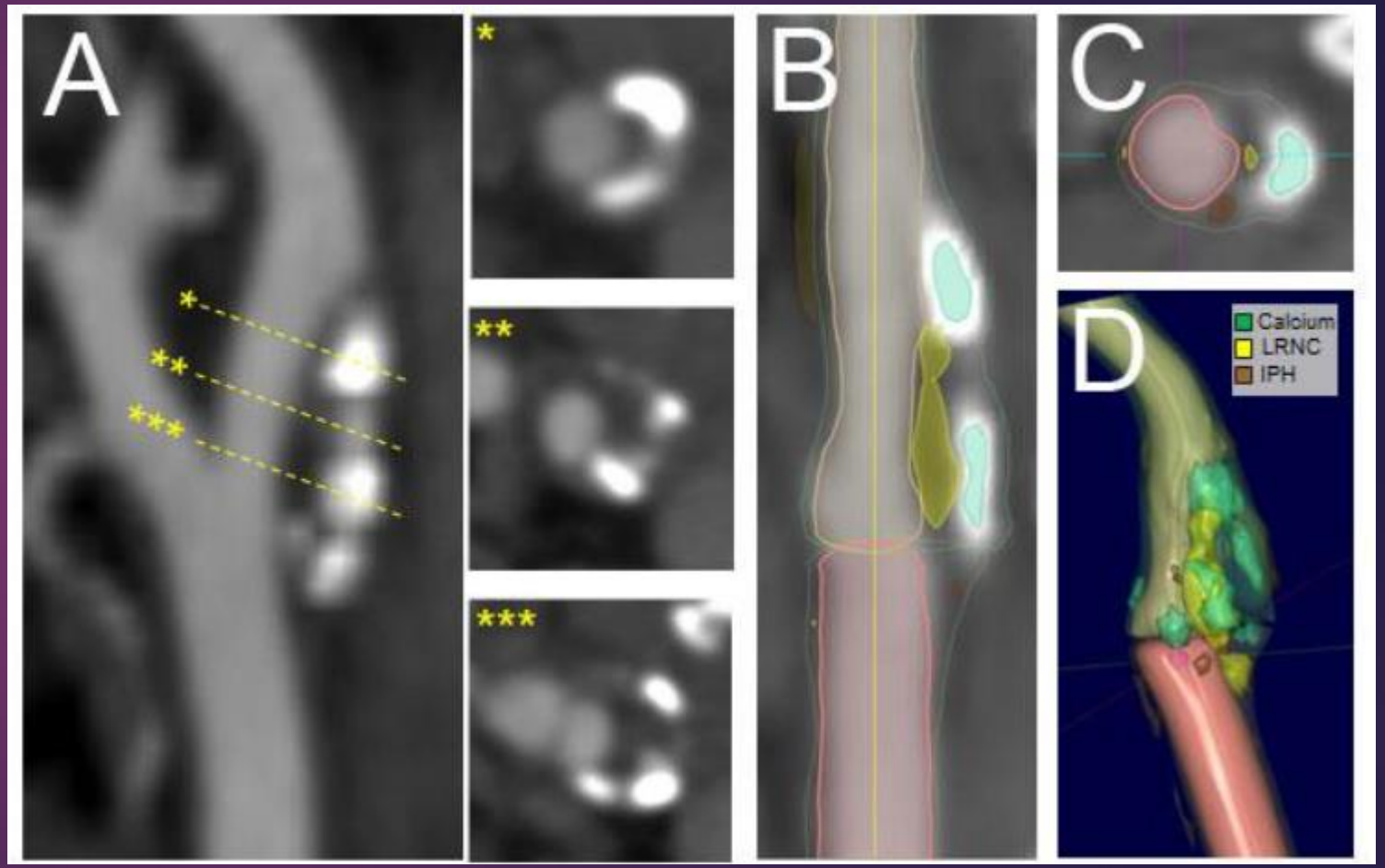
# Methods: Image Segmentation

- A neuroradiologist blinded to the clinical data and side of cerebral infarction segmented each carotid artery (2 cm above/below the bifurcation) using a semi-automated plaque quantification software (Elucid Bioimaging).
- Automated outcomes outputted by the software and used for analysis included volumes of plaque subcomponents (calcium, intraplaque hemorrhage [IPH], and lipid rich necrotic core [LRNC]) and total plaque.

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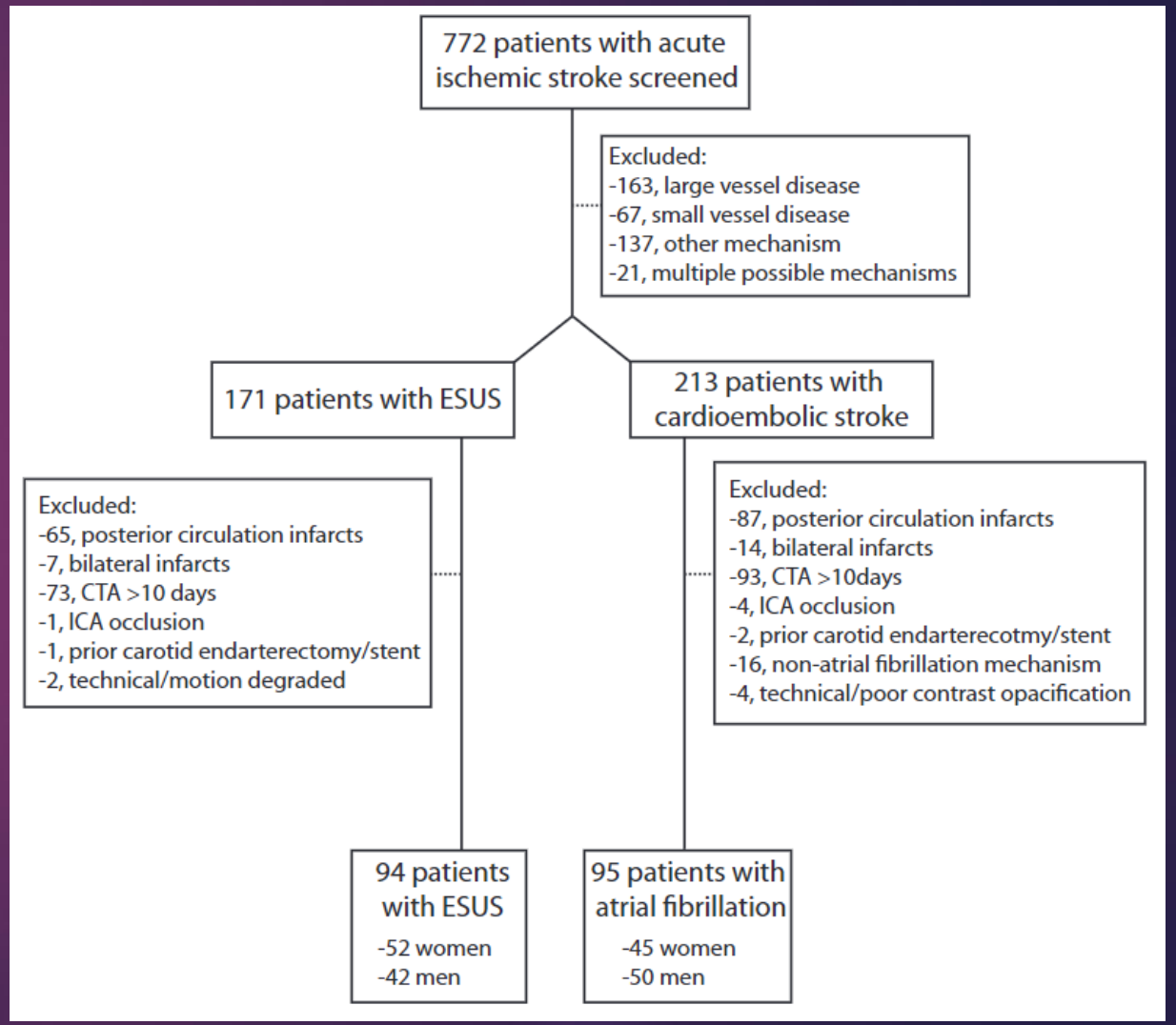
# Results

- Among 772 screened patients, 94 met inclusion criteria for ESUS and 95 had confirmed AF.
- Women had significantly higher BMIs compared to men in the ESUS cohort (p=0.02). The baseline NIH Stroke Scale was significantly higher in women than men in the AF cohort. Otherwise, there were no significant differences in baseline characteristics by sex in the ESUS and AF cohorts.

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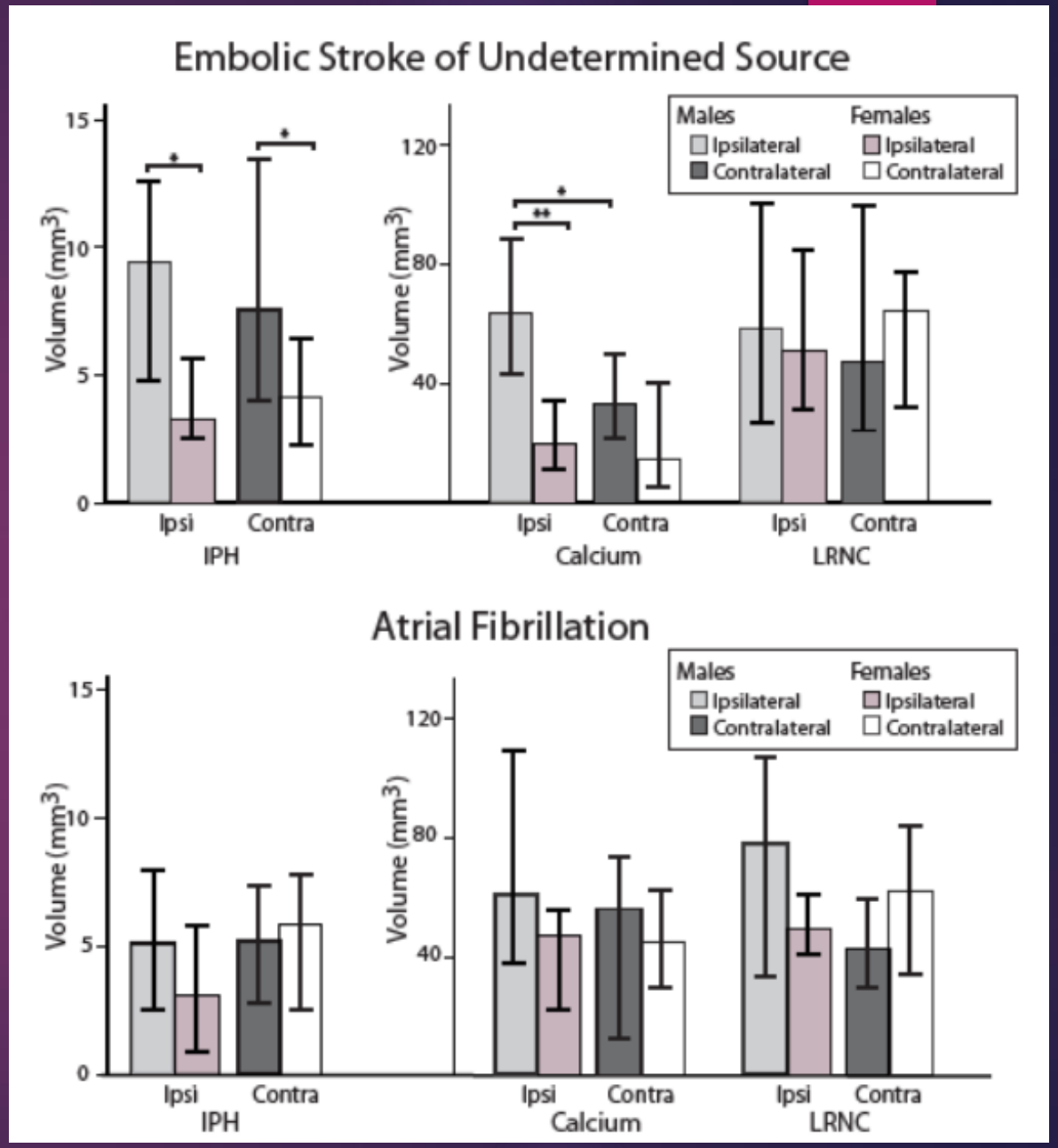
# Results

- Women with ESUS showed significantly lower calcium$_{ipsi}$ and IPH$_{ipsi}$ volumes ($p<0.001$).
- Women also showed lower LRNC$_{ipsi}$ volumes than men though this did not reach statistical significance.
- In the AF cohort, there was no significant difference by sex in carotid plaque composition ipsilateral to stroke side.




Bar graphs represent medians with 95% confidence intervals.
*p<0.05; **p<0.001

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# Discussion

- The results show sex-differences in carotid plaque composition in men versus women with ESUS.
- Women with ESUS had significantly lower volumes of calcified plaque and IPH volumes in carotid arteries ipsilateral to stroke side compared to men.
- This association of high-risk plaque features was not seen in carotid arteries contralateral to the side of stroke in ESUS nor in carotid arteries ipsilateral to stroke side in the AF control sample.
- These results support that non-stenotic carotid plaque contributes to anterior circulation stroke in patients with ESUS and additionally suggest a differential contribution of atheroembolism from carotid plaque in men and women with ESUS

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***Thank you for your attention.***