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Ex Vivo Thrombus Magnetic Resonance Imaging Features and Patient Clinical Data Enable Prediction of Acute Ischemic Stroke Cause

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Stroke: Vascular and Interventional Neurology

RESEARCH LETTER

Ex Vivo Thrombus Magnetic Resonance Imaging Features and Patient Clinical Data Enable Prediction of Acute Ischemic Stroke Cause

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The cause of ischemic stroke often remains elusive even after full stroke workup is completed. Cardioembolic mechanisms in particular are frequently presumed but challenging to definitively diagnose. Quantitative thrombus texture analysis is emerging as a powerful tool for stroke characterization, having shown the ability to predict response to stroke treatment,[1] but its ability to predict stroke cause and complement machine learning models built from standard clinical features has not been studied.[2,3] The purpose of this study is to evaluate the ability of radiomics features extracted from quantitative magnetic resonance images of retrieved ischemic stroke thrombi ($R_2^*(=1/T_2^*)$, quantitative susceptibility mapping, and fat fraction) to improve the accuracy of machine learning models built from clinical data for the prediction of cardioembolic stroke.

METHODS

Institutional research ethics board approval was obtained for this study; data are available from the corresponding author on reasonable request.

Patients with acute ischemic stroke with cardioembolic or large artery atherosclerosis causes determined using TOAST criteria and thrombi retrieved through endovascular therapy were consecutively enrolled into training (February 2016–November 2017; N=49) and validation (November 2019–March 2020; N=11) cohorts. Summary clinical details of each cohort are included in Supplemental Table SI (available from: ir.lib.uwo.ca/vascularpub/59). Patients or their substitute decision-maker gave informed consent after the procedure was completed and ≥1 thrombi were retrieved. A dual-echo-train gradient echo

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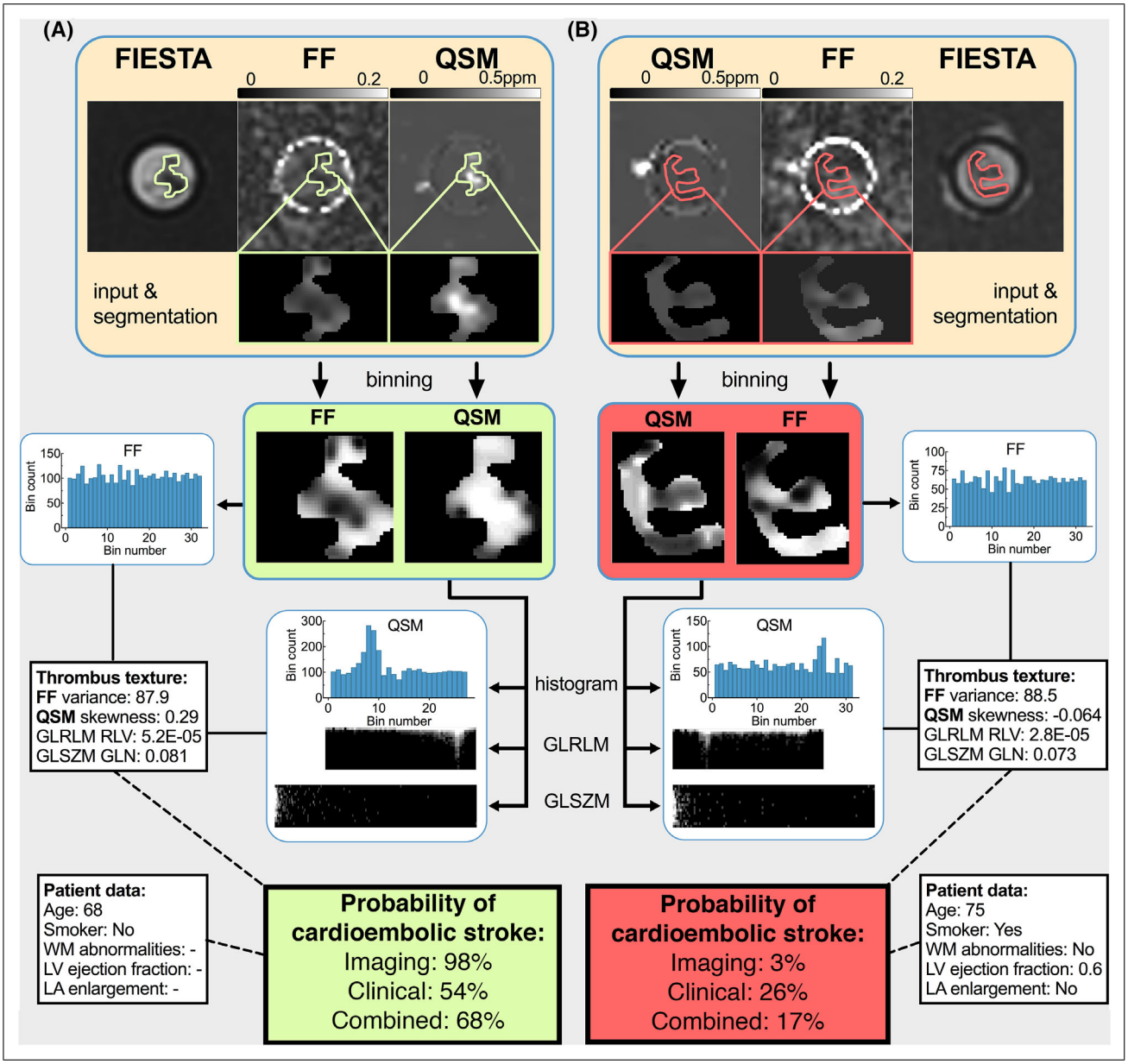

Figure 1. Overview of model processing steps for representative cardioembolic (A) and large artery atherosclerosis (B) thrombi. Segmentations derived from FIESTA-C images are applied to naturally coregistered quantitative susceptibility mapping (QSM) and fat fraction (FF) maps, which are binned before extraction of the histograms and matrices used to derive the 4 predictive texture features for model input. In (A), a patient with known atrial fibrillation did not undergo echocardiography and was missing multiple variables included in the clinical model, uncommon in this cohort but typical of clinical data in general, which resulted in a weak cardioembolic cause prediction that was greatly improved through the addition of thrombus texture information. In (B), all patient clinical features were available and the addition of thrombus texture information improved the model's confidence in the identification of a noncardioembolic cause. GLN indicates gray-level nonuniformity; GLRLM, gray-level run-length matrix; GLSZM, gray-level size zone matrix; LA, left atrial; LV, left ventricular; RLV, run-length variance; and WM, wall motion.

sequence[4] was acquired on the thrombi ex vivo with $0.94 \times 0.94 \times 1.0$ mm^3 resolution and a scan time of 5 minutes 33 seconds on a 3T clinical scanner. A balanced steady-state gradient echo sequence (FIESTA-C) with identical resolution was also acquired and used for thrombus segmentation (scan time: 2 minutes 47 seconds). R_2*, quantitative susceptibility mapping, and fat fraction maps were generated from the multiecho gradient echo data using previously described methods.[4] Random forest classifier models were built to differentiate between cardioembolic and large artery atherosclerosis stroke on a per-thrombus basis using patient clinical data features available from the basic stroke workup and quantitative ex vivo thrombus

magnetic resonance texture features extracted from R_2*, quantitative susceptibility mapping, and fat fraction maps. Models were built in MATLAB (The MathWorks, Inc) using code modified from Vallières et al.[5] Tested texture features are listed in Supplemental Table SII (available from: ir.lib.uwo.ca/vascularpub/59). Feature selection was performed on the training cohort using multivariate logistic regression for texture and univariate statistics for clinical features, respectively. Models were evaluated on the entire validation cohort, and area under the receiver operating characteristic curve (AUC), sensitivity, specificity, and accuracy for all thrombi within the cohort (n=18) were determined.

RESULTS

Within the training cohort, age, smoking, left atrial enlargement, left ventricular ejection fraction, cardiac wall motion abnormalities, and triglyceride levels differed between patients with cardioembolic and large artery atherosclerosis (all $P<0.05$; Supplemental Table SIII, ir.lib.uwo.ca/vascularpub/59) and were thus included in the clinical model. This model predicted cardioembolic mechanism in the validation cohort with an AUC of 0.80 (95% CI, 0.45–1), sensitivity of 80% (95% CI, 52%–100%), specificity of 100%, and accuracy of 91% (95% CI, 78%–100%). Selected thrombus imaging texture features were quantitative susceptibility mapping global skewness, gray-level run-length matrix run-length variance, gray-level size zone matrix gray-level nonuniformity, and fat fraction global variance, and their inclusion increased model AUC, sensitivity, and accuracy to 0.89 (95% CI, 0.68–1), 88% (95% CI, 65%–100%), and 94% (95% CI, 84%–100%), respectively, while maintaining 100% specificity. A separate model built using only thrombus texture features produced an AUC, sensitivity, specificity, and accuracy of 0.63 (95% CI, 0.35–0.9), 75 (95% CI, 45%–100%), 60 (95% CI, 30%–90%), and 67% (95% CI, 45%–89%), respectively. A diagram displaying the texture feature extraction process for 2 representative thrombi and demonstrating the ability for imaging information to improve clinical model predictions is shown in Figure 1.

DISCUSSION

This study suggests that thrombus magnetic resonance imaging can improve the accuracy of clinical data for the prediction of cardioembolic stroke mechanisms. The combination of thrombus imaging texture and baseline clinical data features discriminated between stroke sources with exceptional accuracy.

Recently, a large study by Kamel et al[2] developed a machine learning model for stroke cause prediction using only clinical variables. Similar to our study, the model identified age, left atrial enlargement, ejection fraction, and smoking history as important predictors of cardioembolic cause, and yielded an AUC of 0.85 akin to our clinical-only model. Here, the addition of imaging features improved the performance of the clinical model, suggesting that thrombus imaging information can complement clinical data for this task. This study is limited by its small sample size and ex vivo design; only patients who underwent successful endovascular therapy could be included and alterations to thrombi during thrombolysis, retrieval, or storage could have affected the imaging values. The study is also limited by the lack of a histological validation of imaging features and the inclusion of multiple cardioembolic stroke subtypes in the cardioembolic group. The generalizability of the model to thrombi imaged in vivo remains to be evaluated. Nonetheless, this proof-of-concept study suggests that thrombus magnetic resonance texture features can improve the accuracy of clinical features alone for predicting cardioembolic cause among patients with acute ischemic stroke.

ARTICLE INFORMATION

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Supplemental Materials

Supporting Information.
Tables SI–SIII

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