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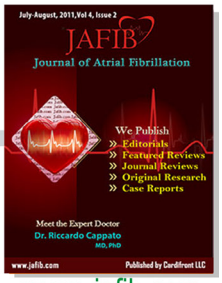

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Association of Left Atrial Fibrosis Detected by Delayed Enhancement Magnetic Resonance Imaging and Risk of Stroke in Patients with Atrial Fibrillation

Dana C. Peters

Original Paper Reviewed
Daccarett M, Badger TJ, Akoum N, Burgon NS, Mahnkopf C, Vergara G, Kholmovski E, McGann CJ, Parker D, Brachmann J, Macleod RS, Marrouche NF. Association of left atrial fibrosis detected by delayed-enhancement magnetic resonance imaging and the risk of stroke in patients with atrial fibrillation. J Am Coll Cardiol. 2011 Feb 15;57(7):831-8

Introduction

This is a review of a recent paper by Daccarett et al,[1] investigating LA remodeling, as assessed by magnetic resonance imaging (MRI), as a risk factor for stroke. A major motivation for treatment of atrial fibrillation (AF) is to reduce the risk of stroke, which often arises from emboli formed in the static left atrium (LA). Risk stratification for stroke in AF patients, important because it determines the use of anti-coagulants in patients, is clinically performed using the validated $CHADS_2$ score (based on prior stroke, diabetes, hypertension, advanced age, and congestive heart-failure). However, because of its limited predictive power, patients with low, moderate and high risk $CHADS_2$ scores are often prescribed anti-coagulants in equal frequencies.[2] There is growing evidence that the burden of AF (i.e. the amount of time that patient remains in AF rhythm) may be a predictor of stroke,[3] since during this time emboli can form in the LA appendage.[4]

Recent important studies from the Utah group[5-7] have demonstrated the potential for cardiac MRI to non-invasively visualize and quantify the scarring in the remodeled LA of patients with AF, generating intense interest from the MRI and EP communities. The MRI technique, called the delayed enhancement [8,9] visualizes the amount of contrast agent retained in the myocardium at a delayed time (10 - 30 minutes) after contrast injection, with more retention indicating scar. The method has been adapted from left ventricular myocardial studies to the imaging of scar in the thin LA wall [10, 11] by increasing the spatial resolution. The imaging of LA scarring may be a surrogate for AF burden, since the AF itself may cause the LA remodeling. Therefore Daccarett et al. investigated this metric as a risk factor for stroke.In their investigation, Daccarett et al1 studied the predictive power of MRI scar assessment to retrospectively predict stroke. They imaged 387 patients with MRI, 9.3% of whom had a previous stroke on average 2 years prior to imaging. The population consisted of equal numbers of subjects in $CHADS_2$ low, intermediate and high risk score categories, with 50% of low risk patients on Warfarin. Their MRI technique used 0.1mmol/kg of Gd-BOPTA, and a 3D

Corresponding Address : Dana C Peters, PhD, Yale School of Medicine, Magnetic Resonance Research Center, TAC N 117, PO Box 20843, New Haven CT 06519.

delayed enhancement sequence with cardiac- and respiratory motion-gating, and 1.3 x 1.3 x 2.5 mm3 resolution with data acquired 15 minutes after injection of contrast. The images were analyzed using manual contouring of the LA walls, and threshold techniques to identify scar. With MRI, they found that the percent of the LA wall which was remodeled was 24% in patients with stroke, vs. 16% in patients without stroke ($p<0.001$). Other variables predictive of stroke included female gender, but not type of AF, diabetes, hypertension, age or congestive heart-failure. The amount of scarring in the LA wall by MRI also correlated with CHADS2 score. When patients were sorted into quartiles, according to percent of the LA wall exhibiting scar by MRI, 3% of stroke patients had the least amount of scarring (Stage 1, <8.5% of the wall), while 53% of stroke patients were found to have the highest amount of scarring (Stage IV, >21%). They performed a multivariate analysis of risk factors for stroke, and found LA remodeling by MRI was an independent predictor of stroke, when the other CHADS variables (CHADS2 excluding prior stroke) were included, and that the area under the curve increased from 0.58 with just CHADS to 0.72 with CHADS+LA structural remodeling. They conclude that LA structural remodeling is a determinant of thrombo-embolism in AF patients, and could be used in conjunction

with clinical variables to risk-stratify patients. This is a large trial, with the important result that AF burden, as assessed by MRI, may improve thrombo-embolic risk stratification in patients. As acknowledged by the authors, one limitation of their study is that the MRI was performed on average 2 years after the stroke, while the clinical goal is to determine whether LA remodeling assessed by MRI predicts future stroke. Therefore, a prospective study is needed. The long-term outcome of the patients without stroke who enrolled in this study will be valuable for this prospective analysis of LA structural remodeling as a risk factor for stroke. Impressive data have been previously presented by the same group, showing correlations between LA remodeling extent by MRI (by blinded analysis) and type of AF, LA size, and AF recurrence.[5,7] This data is in agreement with invasive electrophysiological studies measuring LA scar burden by voltage mapping.[13,14] These studies did not categorize the patients into quartiles based on stage of remodeling, but used more lopsided categories, so that very few patients had extensive remodeling,[5-7] and with that categorization one study showed that stroke was not correlated with LA remodeling by MR.[16] As a note of caution, the MRI delayed enhancement technique employed here for visualizing LA fibrosis due to remodeling has not yet been validated against the gold standard—pathology.The visualization of LA scar due to remodeling stretches the limits of the MRI technique, because the LA wall is thin, and the scar may be partial,[12] and therefore less prominent than scar from ablation or myocardial infarct. Furthermore, the true spatial resolution of the method is limited by signal to noise ratio, cardiac and respiratory motion, and imaging time, and possible imaging artifacts, so that scar in the thin LA wall isn't well-resolved and depends on image quality. Therefore, the basis of their current work–that MRI can identify LA remodeling –is exciting but still controversial, and further validation is essential. In summary, Deccarett et al. demonstrate the value of a novel MRI index in risk-stratification for stroke.Validation of the delayed enhancement MRI for assessing LA remodeling, combined with a prospective study correlating LA remodeling to future stroke, may lead to improved stroke risk-stratification, and guide the use of anti-coagulants

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