MRI Flags Atria Prone to Relapse of Fibrillation

BY MITCHEL L. ZOLER

BOSTON — Researchers recently devised a way to visualize fibrotic tissue within the left atrial wall noninvasively with MRI. Results from a new study that took this analysis a step further showed that patients with atrial fibrillation whose left atrium had high levels of fibrosis also faced a significantly increased risk of failing treatment by pulmonary vein isolation and septal debulking and revert to fibrillation.

The new method of left atrial assessment with delayed-enhancement (DE) MRI may identify patients at the highest risk of early recurrence of atrial fibrillation following a noninvasive, pulmonary-vein isolation procedure, Dr. Saul Kalvaitis said at the Heart Rhythm Society's annual meeting.

Although this early finding needs replication by other groups, it has significant therapeutic implications, said Dr. Melvin M. Scheinman, professor and cardiac electrophysiologist at the University of California, San Francisco. The report suggests that DE MRI may identify patients with atrial fibrillation who are not good candidates for ablation therapy because of high fibrosis content within the atrial wall. Recent research findings by other groups suggest that certain drug treatments reverse fibrosis. If such treatments prove effective, potentially nonresponsive atrial fibrillation patients might benefit from ablation, he added.

DE MRI is now a standard method for assessing ventricular scar tissue, but Dr. Kalvaitis and his coworkers at the University of Utah, Salt Lake City, are the first to apply the method to left atrial assessment, Dr. Scheinman said in an interview. A published report of the Utah group's success with DE MRI for left atrial assessment appeared earlier this year (Circulation 2009;119:1758-67). DE MRI involves infusing gadolinium contrast into the patient. Uptake of the contrast into fibrotic tissue occurs at a different rate compared with its entry into healthy tissue, and this difference allows assessment of the amount and location of fibrotic scar within the heart wall.

In the new study, Dr. Kalvaitis and his associates performed DE MRI exams on 62 patients with atrial fibrillation scheduled to undergo pulmonary vein antrum isolation and atrial septum debulking. Their average age was 64 (range 23-84), and two-thirds were men. On average for the entire group, structural modeling affected 17% of the left atrium.

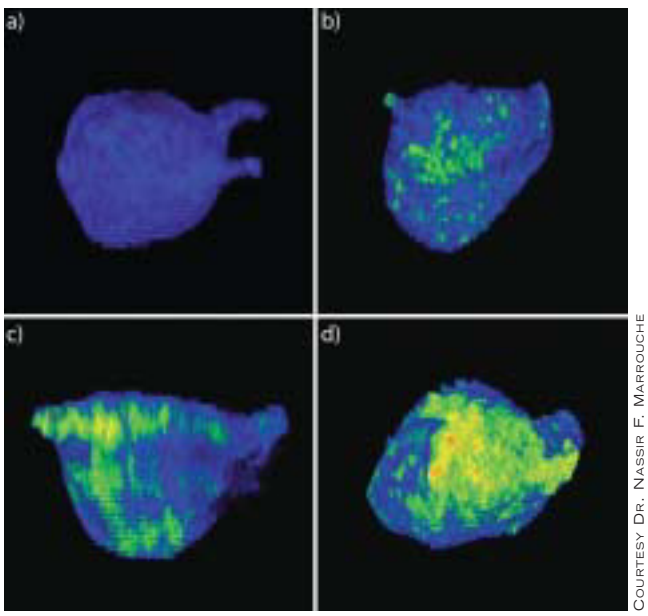
The researchers divided the patients into three subgroups based on the extent of their left atrial remodeling ratio: less than 15% (27 patients), 15%-35% (28 patients), and more than 35% (7 patients). The amount of left atrial fibrosis closely correlated with the ratio of left atrial remodeling, ranging from a mean of 8% fibrosis in patients with the least remodeling to 46% in patients with the most. (See box.)

The incidence of an early recurrence of atrial fibrillation, defined as atrial fibrillation recurring within 3 months of the ablation procedure, closely correlated with the extent of left atrial fibrosis. The early recurrence rate was 19% in the subgroup with the lowest level of atrial fibrosis and 39% and 40%, respectively, in the two subgroups with higher amount of fibrosis.

In a multivariate analysis that controlled for baseline differences among the patients, the subgroup assignment of left atrial remodeling ratio and left atrial fibrosis was the only significant determinant of recurrence risk, increasing the risk by more than twofold, Dr. Kalvaitis reported.

Expressed another way, patients with an early recurrence of atrial fibrillation after ablation had an average 24% left atrial remodeling ratio prior to ablation treatment, compared with an average 14% ratio among those who did not have an early recurrence.

This method for defining recurrence risk may identify patients who would benefit from treatment with an antiarrhythmic drug after ablation, Dr. Kalvaitis said. He said that he and his associates had no financial disclosures. ■



COURTESY DR. NASSIR F. MARROUCHE

Delayed-enhancement MRI images of left atria show fibrotic tissue as green and healthy tissue as blue.

Left Atrial Fibrosis and Recurrent Atrial Fibrillation

Left atrial remodeling ratio	Average fibrosis	Early atrial fibrillation recurrence*
<15% (n = 27)	8%	19%
15%-35% (n = 28)	19%	39%
>35% (n = 7)	46%	40%

*Within 3 months of pulmonary vein isolation.
Note: Based on a study of 62 patients with atrial fibrillation.
Source: Dr. Kalvaitis

ELSEVIER GLOBAL MEDICAL NEWS

Erythropoietin Helpful in Treating Anemia of Heart Failure

BY BRUCE JANCIN

BARCELONA — Erythropoietin therapy in patients with anemia of heart failure resulted in improved exercise capacity, reduced heart failure symptoms, and decreased hospitalizations, and showed strong trends for reduced rates of MI and all-cause mortality in a meta-analysis of 11 small randomized clinical trials.

Moreover, erythropoietin was not associated with an increased rate of adverse events, as in some clinical trials carried out in the settings of cancer or chronic kidney disease. It may be that erythropoietin's angiogenesis-promoting effect is therapeutic in the context of heart failure but is the source of side effects in patients with cancer or renal disease, Dr. Dipak Kotecha said at the annual congress of the European Society of Cardiology.

He was quick to offer a caveat, however: "This is all based on a relatively small sample size. Some of these trials were small proof-of-concept trials; others were mechanistic and looked at the effects of different doses. None were individually powered for clinical events. The follow-up was relatively short, at 2-12 months."

The 11 randomized trials involved 794 patients with mild to moderate anemia and left ventricular systolic heart failure. Nine of the trials were placebo controlled. Mean baseline hemoglobin was 10.1-11.8 g/dL and rose by 2.0 g/dL in response to erythropoietin therapy.

This 2.0 g/dL increase in hemoglobin was associated with a mean 69-meter improvement in 6-minute walk distance compared with controls, a 96-second increase in exercise duration, and an improvement in New York Heart Association functional class equivalent to three-quarters of a class.

"All of these changes were clinically as well as statistically highly significant," observed Dr. Kotecha of Royal Brompton Hospital, London.

Peak oxygen consumption, or VO_2 max, increased by an average of 2.3 mL/kg per minute. Left ventricular ejection fraction increased in erythropoietin-treated patients by an absolute 5.8% compared with controls; that is comparable to the improvement seen in the major clinical trials of beta-blockers. Quality of life scores using the standard Minnesota and Kansas City instruments showed significant gains as well.

Heart failure hospitalizations in erythropoietin-treated patients were significantly reduced by 36% compared with controls, reflecting an absolute 8% rate difference. "The absolute 8% decrease in hospitalizations for heart failure is very similar to what's been seen in the major clinical trials of beta-blocker therapy in heart failure," Dr. Kotecha said.

B-type natriuretic peptide levels fell by an average of 40%, or 237 pg/dL, in response to erythropoietin. Again, that is a magnitude of effect similar to what has been seen in clinical trials of combined beta-blocker and ACE inhibitor or angiotensin receptor blocker therapy, he continued.

The risk of all-cause mortality was reduced by 39% in the erythropoietin treatment group, a strong trend that just missed statistical significance. The 27% relative risk reduction in acute MI also was not quite significant. Definitive answers as to whether erythropoietin therapy has a beneficial effect on these key outcomes are anticipated from the ongoing Amgen-sponsored phase III Reduction of Events With Darbepoetin Alfa in Heart Failure (RED-HF) trial, which is randomizing more than 3,000 patients.

In addition to the question of whether erythropoietin-stimulating agents have a favorable impact on rates of death and acute MI in anemic heart failure patients, other key concerns include the optimal dosage and timing of the therapy and the best target hemoglobin. There are also several ongoing randomized trials looking at whether iron therapy is of value—and if so, in what form—in patients with anemia of heart failure.

Anemia occurs in one-third to one-half of patients with heart failure and has been associated with a markedly worse prognosis. Dr. Kotecha cited as an example a Dutch meta-analysis involving more than 153,000 heart failure patients, 37% of whom were anemic. The mortality after a minimum of 6 months of follow-up was 30% in nonanemic patients and 47% among those with anemia (J. Am. Coll. Cardiol. 2008;52:818-27).

Dr. Kotecha reported having no financial conflicts of interest in connection with the meta-analysis, which was conducted using Cochrane Collaboration methodology and has been submitted to the Cochrane Review for possible publication. ■