#### Editorial / Editöryal Yorum

# Left atrial fibrosis affects left ventricular systolic function in patients with atrial fibrillation

## Sol atriyal fibrozis atriyum fibrilasyonlu hastalarda sol ventrikül sistolik fonksiyonu etkiler

#### Elif Eroğlu, M.D.

Department of Cardiology, Yeditepe University Faculty of Medicine, Istanbul

trial fibrillation (AF) is the most frequent ar-Trhythmia encountered in clinical practice, occurring in 1%-2% of the general population.<sup>[1]</sup> The clinical consequences of AF include increased risk of death, thromboembolic complications and heart failure (HF).<sup>[2]</sup> The increased mortality and morbidity associated with AF have triggered continuing research to explore the potential underlying mechanisms of this arrhythmia and to develop new treatment options.<sup>[1-5]</sup> There is a pathophysiological association between AF and left atrial (LA) electrical, structural and functional remodeling that occurs in response to several pathologic processes.<sup>[6-8]</sup> Left atrial structural remodeling is histologically characterized by the excessive deposition of extracellular matrix protein produced by fibroblasts and is specified as atrial fibrosis. Atrial fibrosis plays a significant part in the pathogenesis of AF through several mechanisms, including impaired electrical activity of myocytes, increased chamber stiffness and conduction abnormalities induced by fibrotic tissues.<sup>[8,9]</sup>

Cardiac imaging is of major importance in the assessment and management of AF. Recent advances in technology have increased the interest in LA structural and functional imaging. Late gadolinium enhancement-magnetic resonance imaging (LGE- MRI) is a recently established method for the evaluation of LA fibrosis. Indeed, one of the very first studies was conducted by the authors of an article mentioned

Abbreviations:	
AF	Atrial fibrillation
CAD	Coronary artery disease
HF	Heart failure
LA	Left atrial
LGE-MRI	Late gadolinium enhancement-
	magnetic resonance imaging
LV	Left ventricular
LVEF	Left ventricular ejection fraction

in this editorial. In that study, the authors elegantly demonstrated that LGE-MRI allows the detection and quantification of LA fibrosis, thus structural remodeling, in patients with AF.<sup>[10]</sup>

In the present study, the authors found that patients with AF and extensive LA fibrosis have depressed left ventricular (LV) systolic function, suggesting that structural remodeling in the LA may also trigger remodeling within the ventricular myocardium.<sup>[11]</sup>

Li et al.,<sup>[12]</sup> in a canine experimental model of AF, showed that LA fibrosis is a more prominent characteristic of HF than electrical remodeling.Very recently, Akkaya and his colleagues, in a clinical study, found a greater degree of LA fibrosis in AF patients with LV systolic dysfunction compared to patients with normal left ventricular ejection fraction (LVEF). Furthermore, in that study, patients with a lower de-



gree of LA fibrosis achieved greater LVEF improvement after catheter ablation for AF.<sup>[13]</sup>

Several mechanisms could be responsible for the impaired LV systolic function in AF patients. As the authors commented in their manuscript, LA fibrosis is associated with generalized fibrosis of the LV in AF patients.<sup>[14]</sup> The data from Ling et al.,<sup>[15]</sup> support the present evidence and further demonstrate that there is an independent association between the degree of diffuse LV fibrosis and LVEF in AF patients. Interestingly, in a subset of isolated AF patients, Ling et al. showed diffuse LV fibrosis, suggesting that AF itself may independently contribute to adverse cardiac remodeling. Although the manuscript from Akkaya and his colleagues does not provide data about LV fibrosis, one can associate myocardial fibrosis with LV systolic function. Another interesting point of view could be that the diffuse LV myocardial fibrosis may also reflect the presence of an underlying cardiomyopathy that antecedes and contributes to the development of AF. However, it would be difficult to test this hypothesis in Akkaya et al.'s manuscript, as 20% of the study population had coronary artery disease, the presence of which was found as one of the significant parameters affecting LVEF.

In conclusion, MRI assessment of LA structural remodeling enables a refinement in the risk stratification of patients with AF. The association between the degree of LA fibrosis, interatrial septal thickness and LV systolic dysfunction is an important clinical issue that remains to be clarified in future studies.

### Conflict-of-interest issues regarding the authorship or article: None declared

#### REFERENCES

- A. John Camm, Paulus Kirchhof, Gregory Y.H. Lip, Ulrich Schotten, Irene Savelieva, Sabine Ernst, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J 2010;31:2369-429. CrossRef
- Stewart S, Hart CL, Hole DJ, McMurray JJ. A populationbased study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. Am J Med 2002;113:359-64. CrossRef
- Lloyd-Jones DM, Wang TJ, Leip EP, Larson MG, Levy D, Vasan RS, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. Circulation

2004;110:1042-6. CrossRef

- Lau DH, Mackenzie L, Kelly DJ, Psaltis PJ, Brooks AG, Worthington M, et al. Hypertension and atrial fibrillation: evidence of progressive atrial remodeling with electrostructural correlate in a conscious chronically instrumented ovine model. Heart Rhythm 2010;7:1282-90. CrossRef
- John B, Stiles MK, Kuklik P, Brooks AG, Chandy ST, Kalman JM, et al. Reverse remodeling of the atria after treatment of chronic stretch in humans: implications for the atrial fibrillation substrate. J Am Coll Cardiol 2010;55:1217-26. CrossRef
- Casaclang-Verzosa G, Gersh BJ, Tsang TS. Structural and functional remodeling of the left atrium: clinical and therapeutic implications for atrial fibrillation. J Am Coll Cardiol 2008;51:1-11. CrossRef
- Allessie M, Ausma J, Schotten U. Electrical, contractile and structural remodeling during atrial fibrillation. Cardiovasc Res 2002;54:230-46. CrossRef
- Yue L, Xie J, Nattel S. Molecular determinants of cardiac fibroblast electrical function and therapeutic implications for atrial fibrillation. Cardiovasc Res 2011;89:744-53. CrossRef
- Kojima T, Kawasaki M, Tanaka R, Ono K, Hirose T, Iwama M, et al. Left atrial global and regional function in patients with paroxysmal atrial fibrillation has already been impaired before enlargement of left atrium: velocity vector imaging echocardiography study. Eur Heart J Cardiovasc Imaging 2012;13:227-34. CrossRef
- Oakes RS, Badger TJ, Kholmovski EG, Akoum N, Burgon NS, Fish EN, et al. Detection and quantification of left atrial structural remodeling with delayed-enhancement magnetic resonance imaging in patients with atrial fibrillation. Circulation 2009;119:1758-67. CrossRef
- Akkaya M, Marrouche N, Higuchi K, Koopmann M, Damal K, Kholmovski E, et al. The degree of left atrial structural remodeling impacts left ventricular ejection fraction in patients with atrial fibrillation. Turk Kardiyol Dern Ars 2014;42:11-9.
- Li D, Fareh S, Leung TK, Nattel S. Promotion of atrial fibrillation by heart failure in dogs: atrial remodeling of a different sort. Circulation 1999;100:87-95. CrossRef
- Akkaya M, Higuchi K, Koopmann M, Damal K, Burgon NS, Kholmovski E, et al. Higher degree of left atrial structural remodeling in patients with atrial fibrillation and left ventricular systolic dysfunction. J Cardiovasc Electrophysiol 2013;24:485-91. CrossRef
- 14. Frustaci A, Caldarulo M, Buffon A, Bellocci F, Fenici R, Melina D. Cardiac biopsy in patients with "primary" atrial fibrillation. Histologic evidence of occult myocardial diseases. Chest 1991;100:303-6. CrossRef
- 15. Ling LH, Kistler PM, Ellims AH, Iles LM, Lee G, Hughes GL, et al. Diffuse ventricular fibrosis in atrial fibrillation: non-invasive evaluation and relationships with aging and systolic dysfunction. J Am Coll Cardiol 2012;60:2402-8. CrossRef