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Clinical value of assessment of left atrial late gadolinium enhancement in patients undergoing ablation of atrial fibrillation

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ABSTRACT

Background: Left atrial (LA) fibrosis begets atrial fibrillation (AF). Cardiovascular magnetic resonance (CMR) using the late gadolinium enhancement (LGE) technique might visualize the LA fibrosis and thus help to choose an appropriate strategy for treatment of AF. In this regard, we investigated whether the extent of preablation LA LGE would predict AF recurrence after ablation in a non-selected patient population.
Methods: CMR was performed in 95 patients before radiofrequency ablation of AF. An interpretable scan was available in 73 patients (age, 59 ± 8 years; men, 71%; persistent/paroxysmal AF, 55/45%). The extent of LA LGE was quantified by three established thresholding techniques. In addition, CMR was used to quantify LA volume and reservoir function. The patients were followed for AF recurrence for 1.3 ± 0.8 years.
Results: The arrhythmia recurred in 29 (40%) of the patients. The extent of LA LGE did not differ between paroxysmal and persistent AF and it did not predict the AF recurrence. Moreover, the extent of LA LGE did not correlate with LA volume, reservoir function and bipolar voltage.
Conclusions: Our data indicate a limited value of a routine assessment of LA LGE before ablation of AF. Further experimental and clinical researches should be done before applying the method to a wide clinical practice.

1. Introduction

Radiofrequency catheter ablation has proved an effective therapy of atrial fibrillation (AF) [1]. Yet, efficiency of the treatment depends mainly on selecting suitable candidates. One possible strategy for stratification of the patients for catheter ablation is to quantify the extent of fibrosis in the left atrium (LA). The rationale for this approach is based on the evidence that more extensive LA fibrosis begets AF [2].

Late gadolinium enhancement cardiovascular magnetic resonance imaging (LGE–CMR) appears a promising tool for assessing of the LA fibrosis in vivo [3]. The study by Oakes et al. and several subsequent studies have demonstrated the use of the LGE–CMR for predicting the clinical outcome of AF ablation [4–7]. But the evidence for use of this technique comes only from a few specialized centers. As a result, assessment of the LA fibrosis by LGE–CMR has not yet been widely adopted in clinical practice.

Our study aimed to evaluate the clinical value of the LA LGE–CMR in a non-selected patient population undergoing ablation for AF. Because the quantification of LA LGE may be biased by inter-individual variability [8], we have quantified the LGE by three different techniques. We expected that patients with more extensive preablation LA LGE would have a higher rate of AF recurrence after ablation. To further evaluate validity of the LA imaging, we investigated the relationship between the LA LGE and other LA characteristics that are pathophysiologically related to the LA fibrosis, such as LA volume, reservoir function and endocardial bipolar voltage.

2. Methods

2.1. Study population

The study included 95 consecutive patients undergoing catheter ablation of AF. Only individuals without a previous ablation and without a contraindication for CMR were included. All patients underwent magnetic resonance imaging within a week before the ablation. After ablation, the patients were followed-up during regular visits at 3 and 6 months, and every 6 months thereafter. Each follow-up examination included 24 h Holter ECG monitoring. In addition, patients who continued complaining of palpitations underwent repeated Holter ECG monitoring (up to 7 days) or monitoring with a portable event recorder, as necessary, until the underlying etiology of the palpitations was clarified. Withdrawal of antiarrhythmics during the follow-up was left on the clinical judgment of the treating physician, who was blinded to the CMR results. AF recurrence was considered only after a post-ablation blanking period of 3 months. The recurrence was defined as any detected episode of AF or atrial tachycardia lasting >30 s [4]. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. All patients gave written consent with the investigation.

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2.2. Cardiovascular magnetic resonance

The imaging was performed on a 1.5 Tesla Scanner (Avanto, Siemens Medical Solutions, Erlangen, Germany) using a 12-channel body coil. A stack of contiguous short-axis cine images of the entire LA was acquired to assess the LA function (typical temporal resolution of 40 ms, voxel size of 2.1 × 1.6 × 8 mm). Subsequently, time-resolved 3D angiography of the LA (voxel size of 1.7 × 1.7 × 1.7 mm) was obtained with a bolus injection of 0.2 mmol/kg of gadobutrol. Acquisition of the LGE images started 10 min after administration of the contrast using a segmented 3D FLASH sequence with FatSat. Typical parameters were: TR/TE of 4.8/1.5 ms, TI of 270 ms, 1 inversion pulse per RR, flip angle of 10°, linear k-space filling, FOV of 400 × 400 × 100 mm, voxel size of 1.6 × 1.6 × 3 mm interpolated to 0.78 × 0.78 × 1.7 mm. The images were acquired during free breathing with a navigator (PACE, acceptance window of ±2.5 mm at end-expiration). ECG-triggering was adjusted using a 4-chamber view cine loop to obtain a subset of images during a cardiac phase with the least LA motion. The average acquisition time for the LGE-MRI study was 11 ± 4 min.

2.3. Image analysis

The extent of the LA LGE was quantified according to Oakes et al. [4] and by additional two automated techniques. First, the LA wall was manually segmented using Slicer 4.2 (Scientific Computing and Imaging Institute, Salt Lake City, Utah). The LA boundaries were anteriorly at the mitral annular plane and posteriorly at the pulmonary vein ostia. The segmented image stack was processed using a custom program written in Matlab. For each slice the program calculated intensity histogram of the voxels belonging to the LA wall. Voxels with intensity values within the 2nd and the 40th percentiles of the histogram (i.e., dark voxels) were classified as a reference tissue. The examiner then interactively selected a threshold at 3, 4 or 5 standard deviations (SDs) above the mean signal intensity of the reference tissue — voxels brighter than the threshold were classified as abnormally enhanced (Fig. 1). The extent of the LA LGE was calculated as the percentage of the abnormally enhanced voxels of all the LA wall voxels. The examiner's choice of the particular threshold was based on the image contrast-to-noise ratio (Fig. 2). The most frequently selected threshold was at 4 SDs (64% of the patients), followed by 3 SDs (19% of the patients) and 5 SDs (17% of the patients).

The second method for quantification of LGE was similar to the method above. However, instead of selecting a threshold by the examiner, a fixed threshold was applied for all patients at 2, 3 and 4 SDs above the mean signal intensity of the reference tissue. Finally, the LGE was quantified by the full-width-at-half-maximum method [8].

LA volume was determined by manual segmentation of the 3D angiogram [9]. LA reservoir function, represented by LA emptying fraction, was assessed on the cine images according to Jarvinen [10].

The images were analyzed by a single CMR specialist (M.S.), who was blinded to the follow-up data. Subjective image quality was assessed at the end of each CMR exam. Scans that contained unidentifiable LA borders or significant artifacts were discarded. To assess intra- and inter-observer reproducibility of the image analysis, 10 scans with an acceptable image quality were re-evaluated by the primary examiner and another two CMR specialists (J.W. and R.K.).

2.4. Catheter ablation

Our method of ablation has been described in detail elsewhere [11]. The procedure was guided by a 3D mapping system (CARTO, Biosense Webster, Diamond Bar, CA) and intra-cardiac echocardiography. Ablation was performed using a 3.5-mm irrigated-tip catheter (NaviStar Thermocool, Biosense Webster, Diamond Bar, CA). The pulmonary veins were isolated by circumferential point-by-point lesions; additional linear lesions were performed in the patients with persistent AF. Radiofrequency energy of up to 35 W was applied at each point for 30–60 s. At the end of the procedure, patients who remained in AF were electrically cardioverted.

A high-density LA voltage map (219 ± 49 equally spaced points) was obtained before ablating. The electrograms were filtered at 30–500 Hz. To correct for the influence of heart rhythm on the electrogram amplitudes, the voltage maps were obtained during either spontaneous or pacing-induced AF. Low-voltage points were defined by two cut-offs: ≤0.2 and 0.5 mV [4,12]. The mean bipolar voltage and the percentage of the low-voltage points were compared with the extent of LA delayed enhancement. All operators were blinded to the CMR results.

2.5. Statistical analysis

Data are reported as the mean ± standard deviation or frequency and percentage. Reproducibility of the LA wall segmentation was evaluated by Dice's coefficient. Agreement between the observers in the quantification of LA LGE was assessed by Pearson's correlation test. Associations between the investigated variables and AF recurrence were explored using Student's t-test or chi-square test, as appropriate. The patients were divided into groups according to the extent of the LA LGE (Table 2). The groups were compared with regard to AF recurrence by one-way ANOVA test. Mutual relationship between the extent of LA LGE, volume, reservoir function and bipolar voltage was analyzed by Pearson's correlation test. P values < 0.05 were considered statistically significant. All analyses were conducted in R (http://www.R-project.org).

3. Results

3.1. Feasibility of LA LGE–CMR

CMR was completed in 91 patients. Of the completed scans, 17 (19%) were corrupted mostly by motion blurring, contrast flow artifacts or diffuse noise (Fig. 3). The artifacts occurred more often in the patients who had AF at the time of the imaging, compared to those who were in sinus rhythm (10 of 30 [33%] vs. 7 of 60 [12%], P = 0.01). In total,

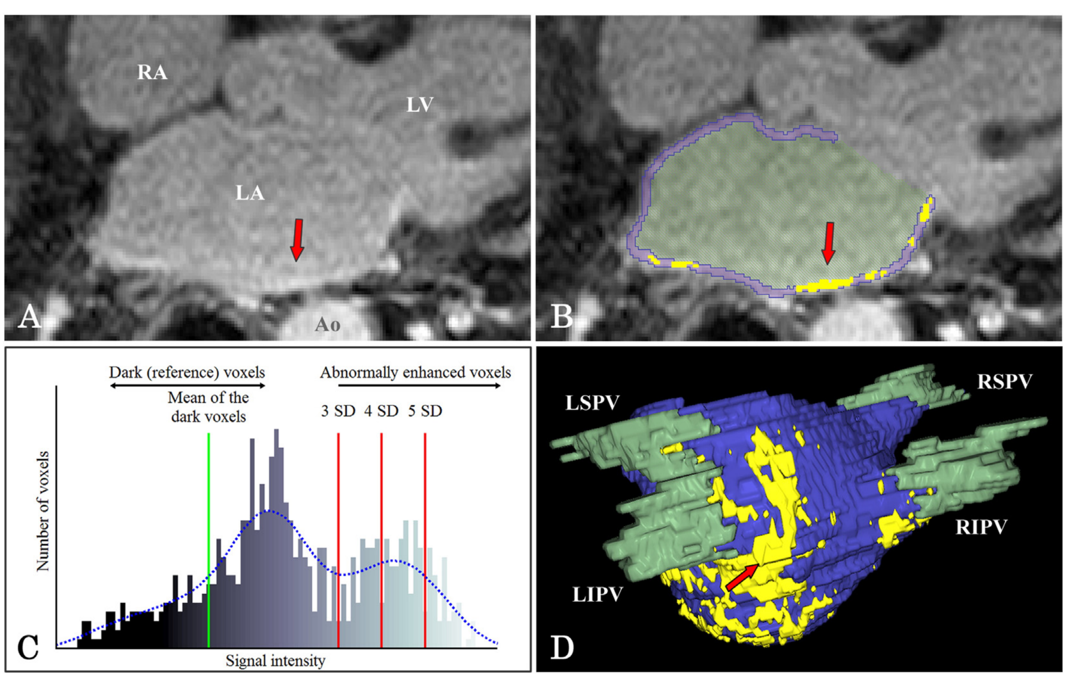

Fig. 1. The figure outlines the principles of the quantification of LA LGE based on the analysis of the image histogram. (A) A native LGE–CMR image of the LA. (B) The identical image with overlaid manual segmentation of the LA wall (blue) and blood pool (green). The areas of LGE (yellow) were identified by the supervised thresholding technique according to Oakes et al. [4]. (C) An image histogram of the LA wall voxels shown on the panel B. The abnormally enhanced voxels are separated from the rest of the LA tissue by arbitrary thresholds. (D) The final thresholded image was reconstructed in 3D using volume surface rendering. The red arrow indicates a corresponding region of abnormal delayed enhancement.