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ORIGINAL PAPER

Prospective evaluation of left atrial function and late gadolinium enhancement with 3 T MRI in patients with atrial fibrillation before and after catheter ablation

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Abstract
In a prospective, randomized study we performed left atrial (LA) functional imaging and late gadolinium enhancement (LGE) in patients undergoing pulmonary vein isolation with ablation of the anterior mitral line to evaluate LA function and visibility of the anterior mitral line and to explore the relationship of these factors to short- and long-term procedural success. Functional imaging of the LA and LGE-visualization 15 min post i.v. administration of gadobutrol was performed on a 3 T MRI system before and after ablation. Patients were grouped in (a) subjects with sinus rhythm, and (b) subjects without sinus rhythm at the follow-up-MRI. Eight patients were excluded due to poor image quality. 37 patients were allotted to group a, 4 patients to group b. Group a showed a significant improvement in ejection fraction (22.3 ± 7.1% vs. 27.2 ± 5.5%; $p < 0.001$), end-systolic volume (111.6 ± 48.3 ml vs. 96.9 ± 37.2 ml; $p = 0.002$), stroke volume (30.2 ± 12.6 ml vs. 35.6 ± 12.6 ml; $p = 0.003$) and LGE (12.5% vs. 83.7%; $p < 0.001$). Group b showed no significant changes in functional parameters or LGE. Patients with successful therapy at 12 months showed significantly lower volumes in the baseline MRI. Scarring along the ablation pathways could be visualized with LGE. Patients with successful CA showed a significant improvement in LA cardiac parameters. Pre-ablation atrial volume seems to be a predictor for long-term success.

Keywords Cardiac MRI · Atrial function · Catheter ablation · Scarring · Anterior mitral line · Gadolinium late enhancement · Atrial fibrillation

Introduction

Atrial fibrillation (AF) is the most common arrhythmia in the western world with a reported incidence of about 0.4% in men and 0.6% in women [1]. It increases the risk for a thromboembolic stroke by about five times and is responsible for about 15% of thromboembolic strokes in Europe and in the USA [2]. Due to the demographic transformation, a doubling to tripling of the incidence is expected in the next 20–30 years [1].

A realistic therapeutic option for AF is catheter ablation (CA) of certain structures in the left atrium (LA) which leads to an isolation of ectopic foci via disruption of the electrical pathways [3]. The most common procedure is pulmonary vein isolation (PVI). Main targets are the pulmonary vein ostia because the myocardial sleeves in these areas are known to be the most common origin of ectopic foci. Another common approach used in combination with PVI are linear ablations whose primary goal is to achieve a bidirectional isolation. One of these lines is the anterior mitral line that is traced from the upper rim of the mitral valve annulus along the bottom of the LA appendage to the upper left pulmonary vein ostium [4].

Late gadolinium enhancement (LGE) is considered the gold standard for fibrosis imaging in the left ventricular myocardium in absence of a histological examination [5, 6]. In the LA global LGE has been associated with structural remodeling in terms of substitution fibrosis [7]. Recently the technique has been applied for the detection of LA scarring after CA with promising results [8].

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In this prospective study, we aimed to investigate short and long-term effects of CA with PVI and ablation of the left anterior mitral line on LA cardiac parameters and to evaluate if the presence of LGE along the ablation pathways shows a correlation to therapy outcome.

Methods

Patients

This single center prospective trial was conducted at the Munich University Hospital and was accepted by the local ethic committee (clinical trial.gov identifier: NCT02217657).

Patients were eligible if ablation for drug resistant persistent AF was planned or if patients presented with AF relapse after PVI for paroxysmal AF and provided written informed consent to participate in the study. Exclusion criteria were: LA thrombi, relevant mitral valve disease (≥ grade 2), impaired left ventricular function (≤ 35%), hyperthyroidism, pregnancy, age < 18 years or > 80 years, known allergy to MR contrast agents, non-MR compatible foreign objects, claustrophobia and declined informed consent.

Magnetic resonance imaging

MRI was performed with a 3 T MR System (Magnetom Verio, Siemens Healthineers, Erlangen, Germany).

Baseline MRI was performed up to 24 h prior to CA. To improve image quality patients in AF underwent external cardioversion before image acquisition. The follow-up MRI was scheduled 3–6 months after CA.

Functional imaging of the LA was performed via steady-state-free-precession cine sequences (slice thickness = 8 mm, time to echo = 1.510 ms, repetition time = 27.440 ms, flip angle = 31°) in the axial view plane. 40 phases were acquired per cardiac cycle. Image evaluation was performed manually by tracing the endocardial contour of the LA in all cardiac phases and then defining the phase with the lowest volume as LA end-systole and the highest volume as LA end-diastole. The LA appendage as well as the pulmonary vein ostia were excluded from the measurements. Exemplary slices for the evaluation of the LA functional parameters are depicted in Fig. 1. For statistical analysis, pre- and post-CA cardiac parameters were assessed.

LGE was visualized with 3D-fast low-angle shot inversion recovery sequences 15 min post intravenous administration of gadobutrol (0.15 mmol/kg bw); (voxel size = 0.9 × 0.9 × 0.9 mm, time to echo = 1.460 ms, repetition time = 462.560 ms, flip angle = 20°, phase sampling = 78%, acquisition matrix = 256/0/0/200 mm). LGE was evaluated in multiplanar reconstructions. Acquisition was performed using ECG and diaphragm triggers. A TI-scout was used to select the optimal inversion time. LGE distribution was evaluated visually. Positive LGE was defined as detection of LGE at the pulmonary vein ostia and at least one segment of the anterior mitral line. The anterior mitral line was divided into three segments; mitral ring to edge of LA appendage, along the LA appendage and edge of LA appendage to pulmonary vein ostium for evaluation of continuity of the ablation scar. The evaluation was performed blinded and randomized in consensus by a cardiologist (10 years' experience in interventional cardiology) and a radiologist consultant (13 years' experience in cardiac MRI). The examiners were blinded to patient information, clinical outcome and time of the examination (pre- or post-CA). An example for the LGE along the ablation pathways is depicted in Fig. 2.

For the results at the time of the follow-up MRI patients were grouped in subjects with successful CA, i.e. sinus rhythm (SR) at the follow-up examination, and subjects without SR at the time of follow-up cardiac MRI.

Image analysis was performed with the Siemens Argus Software (Siemens Healthineers, Erlangen, Germany).

Ablation procedure

Circumferential CA of the PV ostia was performed transseptally using a circular steerable mapping catheter (Lasso™, Biosense-Webster, Diamond Bar, CA, USA) and an irrigated tip ablation catheter (Smart Touch, Biosense Webster). In addition, a LA line from the anterior mitral annulus to the

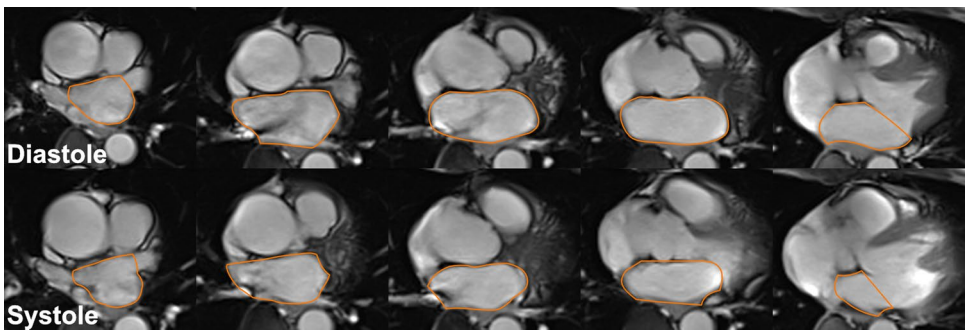

Fig. 1 Segmentation of the LA in systole and diastole. The LA endocardial contour is traced in end-systole and end-diastole excluding the LA appendage and the pulmonary veins

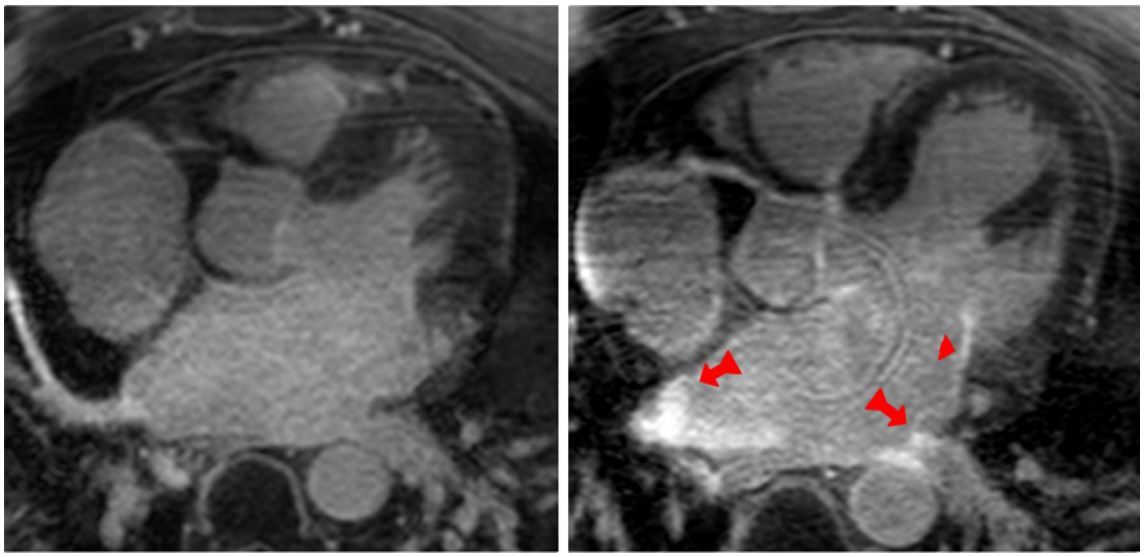

Fig. 2 Pre- and post-ablation cardiac MRI with gadolinium late enhancement in the follow-up examination at the pulmonary vein ostia (arrows) and along the anterior mitral line (arrowhead) in terms of scarring along the ablation pathways

left superior pulmonary vein was drawn. Consecutively bidirectional block was tested using differential pacing criteria and the line was tested for double potentials. Dormant conduction was tested for all PVIs via administration of adenosine after a waiting period of 30 min. Finally, bidirectional conduction block of the anterior line and of all PVs was tested and documented.

Follow up

Clinical follow-ups were performed at the arrhythmia clinic 3, 6, and 12 months after CA. These included extensive questioning for arrhythmia-related symptoms and adverse events. Furthermore, a 7-day Holter-ECG was performed at each visit. Arrhythmic events lasting more than 30 s after a blanking period of 6 weeks post CA were interpreted as arrhythmia recurrence. Follow-up MRI examinations were performed at the 3-month clinical follow-up.

Statistical analysis

Statistical analysis was performed using SPSS (version 24, IBM SPSS Statistics, IBM Corp, Armonk, NY, USA). All values are presented as mean ± SD. Shapiro–Wilks Test was used to test for normality. For the comparison between baseline and follow up MRI Paired *t* test, Wilcoxon's Signed Rank Test and McNemar test were applied for comparisons. For comparison between the two groups at the baseline examination Student's *t* test and Mann–Whitney U test were performed. Sensitivity and specificity were calculated using the McNemar Chi square test. A probability value of $p < 0.05$ was considered statistically significant. The confidence interval, where applicable, was set at 95%.

Results

Study population

72 consecutive patients were included in this prospective study. 13 patients refused further participation in the study and were therefore excluded. Further nine patients were excluded due to the clinical necessity for additional treatment between the two MRI examinations, in eight cases re-PVI, in one case pacemaker implantation. In one case pre-ablation MRI was not performed due to technical difficulties. Pre- and post-ablation MRI was performed in 49 patients. Eight patients were excluded due to poor image quality (breathing artifacts and arrhythmia). Image analysis was performed in the remaining 41 patients. Patient demographics showed no significant difference between both groups in age, gender, diabetes status, hypertension, time since AF diagnosis, time from baseline to follow-up MRI, CHADS-VASc and NYHA score. There was one stroke in the group with successful CA. Detailed information is displayed in Table 1.

Scar detection using late gadolinium enhancement

LGE along the ablation pathways of the left anterior line could be detected in five baseline and in 34 follow-up MRI examinations. This results in a sensitivity of 88% and a specificity of 85%. 23 patients (56%) showed

Table 1 Demographics

	Total	Success at follow-up MRI	Relapse at follow-up MRI	p-value
Female	10 (24%)	10 (27%)	0 (0%)	0.556
Age (years)	65.5 ± 8.8	64.5 ± 8.9	66.0 ± 7.4	0.404
Time since diagnosis (years)	4.9 ± 3.9	4.0 ± 3.2	3.0 ± 8.4	0.687
Ablation to follow-up (days)	98.0 ± 55.3	99.0 ± 58.0	97.5 ± 12.0	0.916
CHADS score	1.9 ± 1.1	2.0 ± 1.1	1.0 ± 0.8	0.091
NYHA stage	0.4 ± 0.6	0.3 ± 0.6	0.5 ± 0.6	0.567
Hypertension	27 (66%)	25 (68%)	2 (50%)	0.596
Diabetes	2 (0.5%)	2 (0.5%)	0 (0%)	1.000
Stroke	1	1	0	1.000

continuity of the left anterior mitral line in LGE. We did not deem our image quality sufficient to evaluate continuity of PVI-scars.

Functional parameters and LGE at baseline MRI

When comparing the baseline parameters between patients with successful CA and AF recurrence at the time of follow-up MRI we could find no significant difference in atrial parameters or the presence of LGE along the ablation pathways.

When comparing the baseline parameters between patients with successful CA and AF recurrence at the 12-month follow-up we found a significantly lower LA end-diastolic volume (LAEDV) (136.0 ± 52.6 ml vs. 178.7 ± 7.2 ml p = 0.031) and LA end-systolic volume (LAESV) (105.9 ± 45.2 ml vs. 145.6 ± 49.4 ml; p = 0.024) in the group with successful CA. This could also be observed with body surface area indexed LAEDV (LAEDVI) (68.5 ± 24.5 ml/m^2 vs. 86.2 ± 23.6 ml/m^2; p = 0.042) and body surface area indexed LAESV (LAESVI) (53.2 ± 20.9 ml/m^2 vs. 70.9 ± 20.6 ml/m^2; p = 0.018).

The detailed results are presented in Table 2.

Successful versus non-successful ablation procedure at the follow-up MRI

Patients with SR at the follow-up MRI showed a significantly higher LA ejection fraction (LAEF) (22.3 ± 7.1% vs. 27.2 ± 5.5%; p < 0.001), LAESV (111.6 ± 48.3 ml vs. 96.9 ± 37.2 ml; p = 0.002), LAESVI (55.3 ± 22.7 ml/m^2 vs. 48.2 ± 17.6 ml/m^2; p = 0.002), LA stroke volume (LASV) (30.2 ± 12.6 ml vs. 35.5 ± 12.6 ml; p = 0.003), indexed LASV (LASVI) (15.1 ± 6.6 ml/m^2 vs. 17.6 ± 5.8 ml/m^2; p = 0.003) and more LGE (5 vs. 31 patients; p < 0.001) from the baseline to the follow-up cardiac MRI. There was no significant difference in pre- and post-ablation LAEDV.

Patients with AF recurrence at follow-up MRI did not show a significant difference in LAEF, LA volumes or the presence of LGE along the ablation pathways. The detailed results are presented in Table 3.

Patients with late AF recurrence

Six patients with SR at the follow-up MRI exhibited AF recurrence up to the 12-month clinical control. In the baseline MRI they showed slightly increased LA volumes with no statistically significant difference when compared to the patients with SR at the 12-month clinical follow-up (LAEDV

Table 2 Comparison of baseline functional parameters and LGE in relation to therapy success at 3 and 12 months

	3 Months		p-value	12 Months		p-value
	Success	Recurrence		Success	Recurrence	
LAEDV (ml)	141.8 ± 55.5	189.9 ± 35.2	0.054	136.0 ± 52.6	178.7 ± 53.7	**0.031**
LAEDVI (ml/m^2)	71.5 ± 25.8	85.0 ± 15.3	0.188	68.5 ± 24.5	86.2 ± 23.6	**0.042**
LAESV (ml)	111.6 ± 48.3	152.9 ± 40.9	0.083	105.9 ± 45.2	145.6 ± 49.4	**0.024**
LAESVI (ml/m^2)	56.4 ± 22.4	68.2 ± 16.4	0.220	53.2 ± 20.9	70.9 ± 20.6	**0.018**
LASV (ml)	30.2 ± 12.6	37.0 ± 5.8	0.133	30.2 ± 12.7	33.2 ± 10.7	0.376
LASVI (ml/m^2)	15.1 ± 6.6	16.9 ± 4.5	0.294	15.3 ± 6.7	15.3 ± 6.0	0.870
LAEF (%)	22.3 ± 7.1	20.4 ± 6.6	0.604	23.0 ± 7.2	19.5 ± 5.7	0.128
LGE (n)	5 (13.5%)	1 (25%)	0.483	5 (16%)	1 (10%)	0.542

Significant results are marked in bold

Table 3 Comparison of functional parameters and LGE in patients with successful therapy versus AF recurrence between baseline and follow-up MRI

	Success		p-value	Recurrence		p-value
	Baseline	Follow-up		Baseline	Follow-up	
LAEDV (ml)	141.8 ± 55.5	132.4 ± 46.8	0.054	189.9 ± 35.2	183.6 ± 58.0	0.735
LAEDVI (ml/m^2)	70.4 ± 26.3	65.8 ± 21.9	0.058	71.8 ± 21.5	68.9 ± 29.1	0.735
LAESV (ml)	111.6 ± 48.3	96.9 ± 37.2	**0.002**	152.9 ± 40.9	147.0 ± 56.2	0.709
LAESVI (ml/m^2)	55.3 ± 22.7	48.2 ± 17.6	**0.002**	58.0 ± 19.0	54.1 ± 25.3	0.310
LASV (ml)	30.2 ± 12.6	35.5 ± 12.6	**0.003**	37.0 ± 5.8	36.5 ± 4.9	0.892
LASVI (ml/m^2)	15.1 ± 6.6	17.6 ± 5.8	**0.003**	13.8 ± 5.3	14.8 ± 5.2	0.735
LAEF (%)	22.3 ± 7.1	27.2 ± 5.5	< **0.001**	20.4 ± 6.6	21.2 ± 5.9	0.467
LGE (n)	5 (12.5%)	31 (83.7%)	< **0.001**	1 (25%)	3 (75%)	0.500

Significant results are marked in bold

128.0 ± 46.7 ml vs. 155.5 ± 43.7 ml; p = 0.190, LAEDVI 68.5 ± 24.5 ml/m^2 vs. 87.1 ± 29.3 ml/m^2; p = 0.147, LAESV 93.4 ± 37.0 ml vs. 114.6 ± 36.0 ml; p = 0.206 and LAESVI 53.2 ± 20.9 ml/m^2 vs. 72.8 ± 24.4 ml/m^2; p = 0.060). Five of these patients demonstrated LGE along the ablation pathways, in addition 2 showed a continuous anterior mitral line in the follow-up MRI. There was no significant difference in LGE along the ablation pathways between patients with maintained SR at 12 months and patients with late AF recurrence.

Discussion

In this prospective blinded study, we explored LA cardiac parameters and LGE prior to and 3 months after PVI and ablation of the anterior mitral line. Patients who remained in SR showed a significant improvement of LAEF, LAESV and LASV. Patients with AF relapse showed no improvement in LA cardiac parameters. Five patients had an LGE in the baseline examination. These patients had previously undergone PVI without isolation of the anterior mitral line and had a relapse of AF. Three of these patients showed an increased LGE at the ablation sites in the follow-up MRI.

A significant increase in LGE in the ablation pathways could only be observed in the group with SR. Six patients with SR at the follow-up MRI showed an AF relapse at the clinical 12-months follow-up. They showed no significant difference in LA parameters or LGE when compared to patients who maintained SR.

Analysis of LGE of the LA is a promising new technique to visualize fibrosis and to evaluate scarring after CA [7–11]. Recent studies show controversial results in LGE after CA. Some authors report a sensitivity and specificity of 100% in fibrosis detection while also being able to evaluate the continuity of the CA scar [10]. Others show less promising results with a sensitivity of 60% and a specificity of 96% in scar detection and a correct identification of lesion distribution in only 28% of patients [11]. Our results showed a sensitivity and specificity of 88% and 85% respectively while we could visualize a continuous LGE along the anterior mitral line in 56% of our patients. We did not deem image quality sufficient to confidently evaluate continuity of the ablation pathway at the pulmonary vein ostia. These discrepancies in lesion detection in the literature may be linked to the duration from CA to image acquisition. LGE-thickness seems to decrease with time as inflammation at the ablation site subsides [10].

Numerous study groups have examined LA cardiac parameters after CA using echocardiography demonstrating an improvement in LA function in patients with successful therapy [12, 13]. Even though cardiac MRI is the gold standard for non-invasive evaluation of cardiac parameters [14] only a few other studies analyzing LA functional parameters with MRI exist. One such study reported a significant decrease in LAEDV, LAESV and a significant increase in LAEF during a 12-month follow-up after PVI [15]. Our study showed no significant decrease in LAEDV in patients with successful CA at the time of the follow-up MRI but observed a significant improvement in LAEF, LAESV and LASV in these patients.

In the same study [15] lower LAEDV in the baseline examination seemed to be a predictor for successful PVI. Our results were congruent with this study only whilst regarding the 12-month clinical examination. Patients who maintained SR after 12 months had significantly lower LAEDV and LAESV than those who had AF recurrence. There was no significant difference in baseline LA cardiac parameters when comparing patients with persisting SR to patients with AF relapse at the time of the follow-up MRI.

To the best of our knowledge our study is the first to analyze LA cardiac parameters in combination with LGE in patients with PVI and CA of the anterior mitral line.

Study limitations

Baseline MRI was performed in < 24 h after external cardioversion which leads to a stunning of the LA. Even though

normalization of LA function can take from a few minutes to a few weeks [16] this should have only little impact on our measurements as patients with AF already exhibit a reduced LAEF. LAEDV in terms of LA dilation should not show any significant change in such a short timeframe.

The number of patients in the group with AF recurrence was low with only four patients at the follow-up MRI and an additional six patients at the 12-months clinical follow-up.

Although we used a 3 T MR tomograph and a slice thickness < 1 mm we were still not able to consistently visualize the ablation pathways to detect discontinuities as a possible cause for AF recurrence. Further possibilities to improve our imaging protocols for future studies should be explored.

Conclusion

PVI with CA of the anterior mitral line leads to a significant improvement of LAEF, LAESV and LASV but not to a reduction in LA dilation in patients who maintain SR. Lower atrial volumes at the baseline examination seem to be a predictor for long-term procedural success. Only the group with successful therapy showed a significantly higher number of patients with LGE along the ablation pathways.

Compliance with ethical standards

Conflict of interest Heidi Estner receives an investigator-initiated grant by Biosense Webster, holds honorary lectures for Boehringer Ingelheim Boston and is an advisory for Boston Scientific. The other authors declare that they have no potential conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Chugh SS, Havmoeller R, Narayanan K et al (2014) Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation 129(8):837–847
2. Ferrari R, Bertini M, Blomstrom-Lundqvist C et al (2016) An update on atrial fibrillation in 2014: from pathophysiology to treatment. Int J Cardiol 203:22–29
3. Kirchhof P, Lip GY, Van Gelder IC et al (2014). Comprehensive risk reduction in patients with atrial fibrillation: emerging diagnostic and therapeutic options–a report from the 3rd Atrial Fibrillation Competence NETwork/European Heart Rhythm Association consensus conference. Europace 14(1):8–27
4. Fichtner S, Sparn K, Reents T et al (2015) Recurrence of paroxysmal atrial fibrillation after pulmonary vein isolation: is repeat pulmonary vein isolation enough? A prospective, randomized trial. Europace 17(9):1371–1375
5. Sandstede JJ, Lipke C, Beer M et al (2000) Analysis of first-pass and delayed contrast-enhancement patterns of dysfunctional myocardium on MR imaging: use in the prediction of myocardial viability. AJR Am J Roentgenol 174(6):1737–1740
6. Setser RM, Bexell DG, O'Donnell TP et al (2003) Quantitative assessment of myocardial scar in delayed enhancement magnetic resonance imaging. J Magn Reson Imaging 18(4):434–441
7. Oakes RS, Badger TJ, Kholmovski EG et al (2009) Detection and quantification of left atrial structural remodeling with delayed-enhancement magnetic resonance imaging in patients with atrial fibrillation. Circulation 119(13):1758–1767
8. McGann CJ, Kholmovski EG, Oakes RS et al (2008) New magnetic resonance imaging-based method for defining the extent of left atrial wall injury after the ablation of atrial fibrillation. J Am Coll Cardiol 52(15):1263–1271
9. Higuchi K, Akkaya M, Akoum N, Marrouche NF (2014) Cardiac MRI assessment of atrial fibrosis in atrial fibrillation: implications for diagnosis and therapy. Heart (Br Card Soc) 100(7):590–596
10. Peters DC, Wylie JV, Hauser TH et al (2007) Detection of pulmonary vein and left atrial scar after catheter ablation with three-dimensional navigator-gated delayed enhancement MR imaging: initial experience. Radiology 243(3):690–695
11. Hunter RJ, Jones DA, Boubertakh R et al (2013) Diagnostic accuracy of cardiac magnetic resonance imaging in the detection and characterization of left atrial catheter ablation lesions: a multicenter experience. J Cardiovasc Electrophysiol 24(4):396–403
12. Beukema WP, Elvan A, Sie HT, Misier AR, Wellens HJ (2005) Successful radiofrequency ablation in patients with previous atrial fibrillation results in a significant decrease in left atrial size. Circulation 112(14):2089–2095
13. Muller H, Noble S, Keller PF et al (2008) Biatrial anatomical reverse remodelling after radiofrequency catheter ablation for atrial fibrillation: evidence from real-time three-dimensional echocardiography. Europace 10(9):1073–1078
14. Sallach SM, Peshock RM, Reimold S (2007) Noninvasive cardiac imaging in pulmonary hypertension. Cardiol Rev 15(2):97–101
15. Jahnke C, Fischer J, Gerds-Li JH et al (2011) Serial monitoring of reverse left-atrial remodeling after pulmonary vein isolation in patients with atrial fibrillation: a magnetic resonance imaging study. Int J Cardiol 153(1):42–46
16. Khan IA (2003) Atrial stunning: basics and clinical considerations. International J Cardiol 92(2–3):113–128