# Blood Flow Volume of Left Atrial Appendage Measured by Magnetic Resonance Imaging is Improved after Radiofrequency Catheter Ablation of Atrial Fibrillation

Yun Gi Kim[1], Kyongjin Min[2], Sung Ho Hwang[3], Jaemin Shim[2], Yun Young Choi[1], Ha Young Choi[3], Jong-Il Choi[3], Yu-Whan Oh[2], and Young-Hoon Kim[4]

[1]Korea University Anam Hospital
[2]Korea University - Anam Campus
[3]Korea University Medical Center
[4]Korea University Medical Centrer

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## Abstract

Introduction: Hemodynamics of left atrial appendage (LAA) is an important factor for future risk of ischemic stroke in atrial fibrillation (AF) patients and velocity encoded cardiac magnetic resonance imaging (VENC-MRI) can evaluate blood flow volume of LAA without any invasive procedures. We aimed to evaluate the impact of radiofrequency catheter ablation (RFCA) on LAA hemodynamics via MRI evaluation. Methods and Results: Consecutive RFCA cases in a single arrhythmia center were retrospectively analyzed. A total of 3,120 AF patients who underwent first RFCA were analyzed. Among these patients 360 patients had both pre- and post-RFCA VENC-MRI evaluation. Atrial fibrillation was non-paroxysmal in 174 (48.3%) patients. Mean VENC-MRI (ml/sec) was significantly improved after RFCA with 49.75±32.97 and 71.92±34.94 for pre- and post-RFCA, respectively. Patients with non-paroxysmal AF ([?]VENC-MRI = 29.71+-35.30 vs. 14.42+-40.94; $p < 0.001$) and low pre-RFCA VENC-MRI ([?]VENC-MRI = 50.64+-28.92 vs. 16.72+-38.39; $p < 0.001$) had significantly higher improvement in VENC-MRI. Those who experienced late recurrence before post-RFCA MRI had significantly less improvement in LAA flow volume ([?]VENC-MRI = 15.55+-41.41 vs. 25.75+-37.00; p = 0.016). Similar results were obtained after adjusting covariates. Conclusions: Radiofrequency catheter ablation can significantly improve hemodynamics of LAA in AF patients. The beneficial effects were most prominent in non-paroxysmal AF, those who had low pre-RFCA VENC-MRI, and those without late recurrence. Whether the improved hemodynamics of LAA after RFCA actually leads to reduced risk of ischemic stroke should be evaluated in future trials.

## 1. Introduction

Atrial fibrillation (AF) is characterized by rapid and disorganized electrical activation of the atrium which leads to loss of efficient atrial contraction.[1, 2] The loss of organized atrial contraction provokes blood stasis especially in the left atrial appendage (LAA) which can be visualized by trans-esophageal echocardiography (TEE) as spontaneous echo-contrast (SEC).[3, 4] The blood stasis can serve as a nidus for thrombus formation leading to clinical stroke, a major complication of AF.[4-8] Evaluation of hemodynamics of LAA is performed with TEE by detecting SEC of measuring LAA flow velocity. However, TEE is an invasive procedure and procedure-related complications such as esophageal injury can occur. Furthermore, most patients require intravenous sedatives due to pain and inconvenience related with insertion of the TEE probe. Magnetic resonance imaging (MRI), a non-invasive test compared with TEE, can measure the flow volume of LAA.[9] Velocity-encoded (VENC) cardiac MRI enables measurement of LAA blood volume during the cardiac cycle and has strong correlation with TEE parameters of LAA hemodynamics.[10, 11] Previous reports revealed that the evaluation of LAA blood flow with VENC-MRI can identify blood stasis in LA and LAA.[10]

The role of radiofrequency catheter ablation (RFCA) in AF patients was largely limited to improvements in the quality of life and subjective symptoms.[12, 13] However, recent studies suggest that the beneficial effect of RFCA extends beyond quality of life.[14-16] Although the reduction of ischemic stroke by RFCA in AF patients has not been demonstrated in randomized clinical trials, various observational studies suggest that RFCA can reduce the risk of ischemic stroke.[15-18]Restoration of sinus rhythm might significantly improve hemodynamics of LAA. In the other hand, scar formation due to radiofrequency energy delivery might have adverse influence on LAA. Impact of RFCA on LAA hemodynamics AF patients is not fully evaluated. We aimed to measure the flow volume of LAA before and after RFCA with VENC-MRI in AF patients.

## 2. Methods

### 2.1 Patients

All RFCA procedures for AF performed in Korea University Medicine Anam Hospital from June 1998 to April 2019 were screened. The Institutional Review Board of Korea University Medicine Anam Hospital approved the study, and written informed consent was waived due to its retrospective nature. The ethical guidelines of the 2008 Declaration of Helsinki were applied to all study protocols.

### 2.2 Cardiac MRI and Image Analysis

Cardiac MRI examinations were performed using a 3T MRI scanner (MAGNETOM Skyra, Siemens Healthineers, Erlangen, Germany) with a phased array 18-channel body matrix coil and 12-channel of the 32-channel spine matrix coil. VENC-MRI was a sequence of cardiac MRI protocol. A retrospective electrocardiography (ECG) gated, two-dimensional flow-sensitive phase-contrast gradient-echo sequence was performed for VENC-MRI perpendicular to the LAA ostium. VENC-MRI parameters were as follows: TR/TE, 4.5 msec/2.9 msec; flip angle, 15°; 30 frames per heartbeat; encoding velocity set, 200 cm/sec; PAT factor, 2. In the analysis of LAA hemodynamics, VENC-MRI data were analyzed by two cardiovascular image experts (S.H.H with 10 years of experience in cardiovascular imaging, and Y.H.O with 23 years of experience in cardiovascular imaging) using a commercial software workstation (Terarecon iNtuition; TeraRecon, Foster City, CA, USA). Both reviewers were blinded to the patients' clinical information. The reviewers traced and determined the outer contours of the LAA ostium and descending aorta on VENC-MRI in consensus to evaluate both the LAA and aortic blood flow in a cardiac cycle. Based on the VENC-MRI data, the development of blood flux peak from the LAA to the LA chamber was defined as a LAA emptying. The maximum blood flux of LAA emptying was defined as the LAA emptying flux (in ml/s).

### 2.3 Ablation procedure

The protocol for RFCA in our institution is described in the previous studies.[19, 20] In brief, double transseptal punctures were performed after positioning multi-polar catheters at the right ventricle, high right atrium, and coronary sinus. The EnSite NavX/Velocity (St. Jude Medical, St. Paul, MN) or CARTO (Biosense Webster, Irvine, CA) system were used for three-dimensional electroanatomic mapping. In patients with paroxysmal AF, the endpoint of the procedure was the elimination of all trigger focus. If non-pulmonary vein trigger was present after successful pulmonary vein isolation, additional ablation was performed to eliminate non-pulmonary vein trigger. Additional substrate modification was performed if the operator considered non-inducibility is more important than trigger point elimination. In non-paroxysmal AF, AF was induced by rapid atrial pacing after pulmonary vein isolation. The procedure was finished if sustained AF (lasting for more than five minutes) was not induced. Additional ablation such as complex fractionated atrial electrogram guided ablation, linear ablation, or low-voltage zone ablation were performed at the operator's discretion if sustained AF was induced after pulmonary vein isolation.

### 2.4 Definitions

Paroxysmal AF was defined as AF which self-terminates within seven days, and non-paroxysmal AF as

AF lasting for more than seven days or requiring direct-current cardioversion for termination. In the current study, atrial tachyarrhythmia consisted of both AF and atrial tachycardia. Late recurrence was defined as any atrial tachyarrhythmia lasting for more than 30 seconds 90 days after RFCA. A single strip (10 seconds) of 12-lead surface electrocardiography showing atrial tachyarrhythmia was also classified as recurrence. Routine Holter monitoring was performed three, six, nine, and 12 months after RFCA. Additional Holter monitoring and portable event recorder evaluation were done whenever needed.

## 3 Statistical analysis

Continuous variables are expressed as mean ± standard deviation and compared with the unpaired t-test. Dependent continuous variables were compared with paired t-test. Categorical variables are expressed as percentile value and compared with the Chi-square or Fisher's exact test as appropriate. Multivariate logistic regression analysis was performed to adjust the influence of covariates. A general linear model (analysis of covariance) was applied to evaluate the impact of RFCA on LAA flow volume while controlling the effect of covariates. Estimated means calculated by general linear model are presented as mean values with 95% confidence intervals. Results were considered to be significant if the p-value was <0.05 on a two-tailed test. All statistical analyses were performed using IBM SPSS Statistics software, Version 24.0 (IBM, Armonk, NY).

## 4 Results

### 4.1 Patients

Study flow of this study is shown in Figure 1. A total of 3,120 patients underwent de-novo RFCA for AF from June 1998 to April 2019 in our institution. Mean age was 55.74 ± 10.96 years and 78.9% were male. The mean $CHA_2DS_2$-VASc score was 1.27 ± 1.26. Non-paroxysmal AF was observed in 1,277 (40.9%) patients. Baseline demographics of our cohort are described in detail in our previous studies.[18, 20] Among 3,120 patients, 360 patients had both pre- and post-RFCA VENC-MRI evaluation. Baseline characteristics of these 360 patients with VENC-MRI are described in Table 1. Mean age was 57.31 ± 11.16 years old and 77.2% were male. Mean body mass index was 25.03 ± 2.92 which is significantly lower compared with RFCA cohorts of western countries. Atrial fibrillation was non-paroxysmal in 174 (48.3%) patients and mean $CHA_2DS_2$-VASc score was 1.40 ± 1.27.

### 4.2 Impact of RFCA on VENC-MRI

Mean value of pre-RFCA VENC-MRI was 49.85 ± 32.97 which was improved to 71.92 ± 34.94 after RFCA (44.3% improvement; p < 0.001; Figure 2). The degree of improvement in VENC-MRI was more pronounced in non-paroxysmal AF ([?]VENC-MRI = 14.42 +- 40.94 vs. 29.71 +- 35.30; p < 0.001; Figure 2).

In our cohort, 139 patients (38.6%) experienced late recurrence before undergoing post-RFCA VENC-MRI evaluation. Patients without late recurrence had significantly greater improvement in VENC-MRI ([?]VENC-MRI = 15.55 +- 41.41 vs. 25.75 +- 37.00; p = 0.016; Figure 2). In paroxysmal AF, numerically higher but statistically insignificant improvement in VENC-MRI was observed in those without late recurrence ([?]VENC-MRI = 8.46 +- 44.19 vs. 17.77 +- 38.78; p = 0.137; Figure 2). However, [?]VENC-MRI was significantly higher in those without late recurrence in non-paroxysmal AF patients ([?]VENC-MRI = 22.14 +- 37.77 vs. 35.06 +- 32.58; p = 0.017; Figure 2).

Patients with low pre-RFCA (VENC-MRI < 20 ml/sec) VENC-MRI had significantly greater improvement after RFCA ([?]VENC-MRI = 16.72 +- 38.39 vs. 50.64 +- 28.92; p < 0.001; Figure 2). Low VENC-MRI before RFCA was a significant factor associated with greater improvement in VENC-MRI after RFCA in both paroxysmal ([?]VENC-MRI = 9.92 +- 39.50 vs. 62.19 +- 20.76; p < 0.001; Figure 2) and non-paroxysmal AF ([?]VENC-MRI = 25.23 +- 35.30 vs. 45.77 +- 30.68; p = 0.001; Figure 2).

### 4.3 Multivariate model

In univariate analysis, sex, type of AF, late recurrence, LAA flow velocity, and pre-RFCA VENC-MRI was associated with [?]VENC-MRI (Table 2). After including these factors in the multivariate model, late recurrence (unstandardized coefficient = -10.864; $p < 0.001$) and pre-RFCA VENC-MRI (unstandardized coefficient = -0.628; $p < 0.001$) were independent factors associated with [?]VENC-MRI (Table 2).

Estimated means calculated by general linear model (analysis of covariance) is depicted in Figure 3. After adjusting sex, AF type, and pre-RFCA VENC-MRI, late recurrence was independently associated with [?]VENC-MRI: patients without late recurrence had significantly higher improvement in LAA hemodynamics after RFCA ([?]VENC-MRI = 13.80 [8.38 – 19.21] vs. 26.85 [22.56 – 31.15]; $p < 0.001$; Figure 3). Low LAA flow volume (pre-RFCA VENC-MRI < 20 cm/sec) was independently associated with higher improvement in VENC-MRI after RFCA after adjusting the influence of sex, AF type, and late recurrence ([?]VENC-MRI = 17.17 [13.09 – 21.25] vs. 48.13 [38.29 – 57.98]; $p < 0.001$; Figure 3).

## 5 Discussion

This study demonstrated that (i) flow volume of LAA measured by VENC-MRI is significantly improved after RFCA in AF patients; (ii) patients without late recurrence can have significantly greater improvement in LAA flow volume; (iii) the degree of improvement in VENC-MRI is significantly more prominent in patients with low LAA flow volume before RFCA. This is the first study to demonstrate the relationship between RFCA and improvement in VENC-MRI, a reliable predictor of LAA hemodynamics. The strong points of the current study are as follows: (i) measurement of LAA flow volume with MRI, a non-invasive imaging test; (ii) sufficient number of patients who had both pre- and post-RFCA VENC-MRI results.

### 5.1 RFCA and ischemic stroke

Previous observational studies suggest that RFCA can reduce the risk of ischemic stroke in AF patients. A nationwide cohort data from Sweden, RFCA was associated with a 31% reduction of ischemic stroke with the benefit more prominent in AF patients with $CHA_2DS_2$-VASc [?] 2 (hazard ratio = 0.39).[16] Noseworthy and his colleagues reported a 44% reduction in the risk of ischemic stroke for those who met the inclusion criteria of CABANA trial using a retrospective cohort of 183,760 AF patients.[15] The CABANA trial itself disabling stroke occurred in 3 and 6 patients in RFCA and medical treatment group, respectively (hazard ratio = 0.42; $p < 0.19$).[21]The CASTLE-AF trial reported a statistically insignificant 54% reduction in the risk of cerebrovascular accident in RFCA group compared to medical treatment group ($p = 0.014$).[14] Despite statistical insignificance in randomized clinical trials, numerical reduction in the risk of ischemic stroke and lack of statistical power due to small sample size should be taken in to account.

### 5.2 Hemodynamics of LAA

Our data can provide pathophysiologic insight to the potential reduction of ischemic stroke after RFCA: a significant improvement of LAA flow volume after RFCA. In our RFCA cohort including both paroxysmal and non-paroxysmal AF patients, VENC-MRI was increased by 44% after RFCA. Rhythm theory and atrial cardiomyopathy theory are two major explanations for the increased risk of ischemic stroke in AF patients.[2, 18] Although there are no concrete evidence that RFCA can reverse atrial cardiomyopathy, successful maintenance through RFCA will significantly improve the hemodynamics of LAA as demonstrated in this study. In our cohort, those without late recurrence had significantly greater improvement in VENC-MRI ([?]VENC-MRI = 15.55 +- 41.41 vs. 25.75 +- 37.00; $p = 0.016$). Those with low VENC-MRI before RFCA also had greater improvements ([?]VENC-MRI = 16.72 +- 38.39 vs. 50.64 +- 28.92; $p < 0.001$). Our results suggest successful maintenance of sinus rhythm thorough RFCA especially in those with limited LAA function at baseline can have significant positive impact on LAA hemodynamics. Whether this beneficial effect on LAA flow volume will lead to decrease in clinical ischemic stroke needs further investigation.

### 5.3 Benefit of non-invasive imaging

Function of LAA is difficult to measure and transesophageal echocardiography is virtually only available option. Although abnormal LAA function is a known risk factor for ischemic stroke in AF patients, it is not incorporated into $CHA_2DS_2$-VASc scoring system.[4-8, 22] Main reason is that transesophageal echocardiography (i) is an invasive imaging test; (ii) has rare but serious complications such as esophageal injury; (iii) is associated with patient discomfort related with the insertion of the probe usually requiring sedatives; and

(iv) requires well trained cardiologist to perform and therefore is not an anytime available test. Recent studies revealed that LAA flow volume measured with VENC-MRI can reliably predict LAA hemodynamics.[9, 10] Since VENC-MRI is a non-invasive imaging test that do not require inconvenient probe insertion, it has a potential for disseminated use. The role of VENC-MRI in the prediction of ischemic stroke and assessing the result of RFCA in AF patients warrants large randomized clinical trials.

## 6 Limitation

The results of this study are not free from intrinsic limitations of retrospective cohort analysis. No cryoablation cases were included ant the results of the current study are limited to RFCA. Only East Asian patients were included in our cohort and caution is needed when applying the results of this study to different ethnic groups.

## 7 Conclusion

Significant improvement in LAA hemodynamics measured with VENC-MRI were observed in AF patients undergoing RFCA. The beneficial effect of RFCA was more prominent in those without late recurrence and who had impaired pre-RFCA LAA function.

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**Abbreviations**

AF: atrial fibrillation; AT: atrial tachycardia; CI: confidence interval; MRI: magnetic resonance imaging; LA: left atrium; LAA: left atrial appendage; RFCA: Radiofrequency catheter ablation; VENC: velocity-encoded.

**Author contribution statement**

J. Shim had full access to all data in this study and is responsible for data integrity and analytical accuracy. The study concept and design were made by Y. G. Kim, S. H. Hwang, J. Shim, and Y. H. Kim. MRI data acquisition and interpretation was performed by S. H. Hwang and Y. W. Oh. Data analysis and interpretation was performed by Y. G. Kim, K. J. Min, H. Y. Choi, Y. Y. Choi, and J. Shim. Y. G. Kim and K. J. Min drafted the article. S. H. Hwang and J. Shim reviewed and edited the manuscript. Y. G. Kim and K. J. Min performed the statistical analysis.

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**Competing interest statement:** The authors have nothing to disclose.

**Figure Legends**

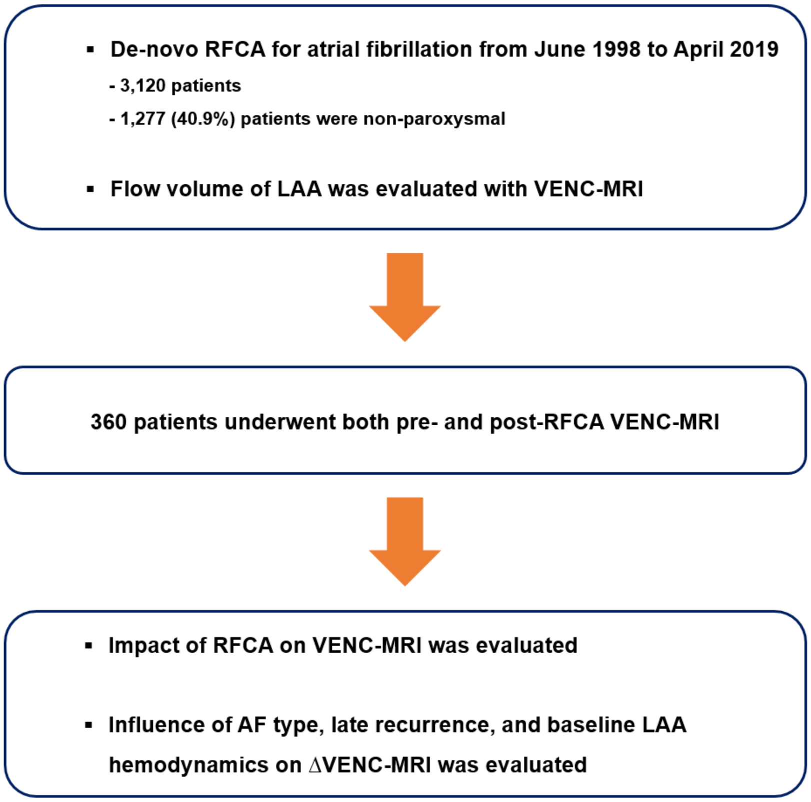


**Figure 1.** Flow of the study.

AF: atrial fibrillation; LAA: left atrial appendage; RFCA: radiofrequency catheter ablation; VENC-MRI: velocity-encoded cardiac magnetic resonance imaging.

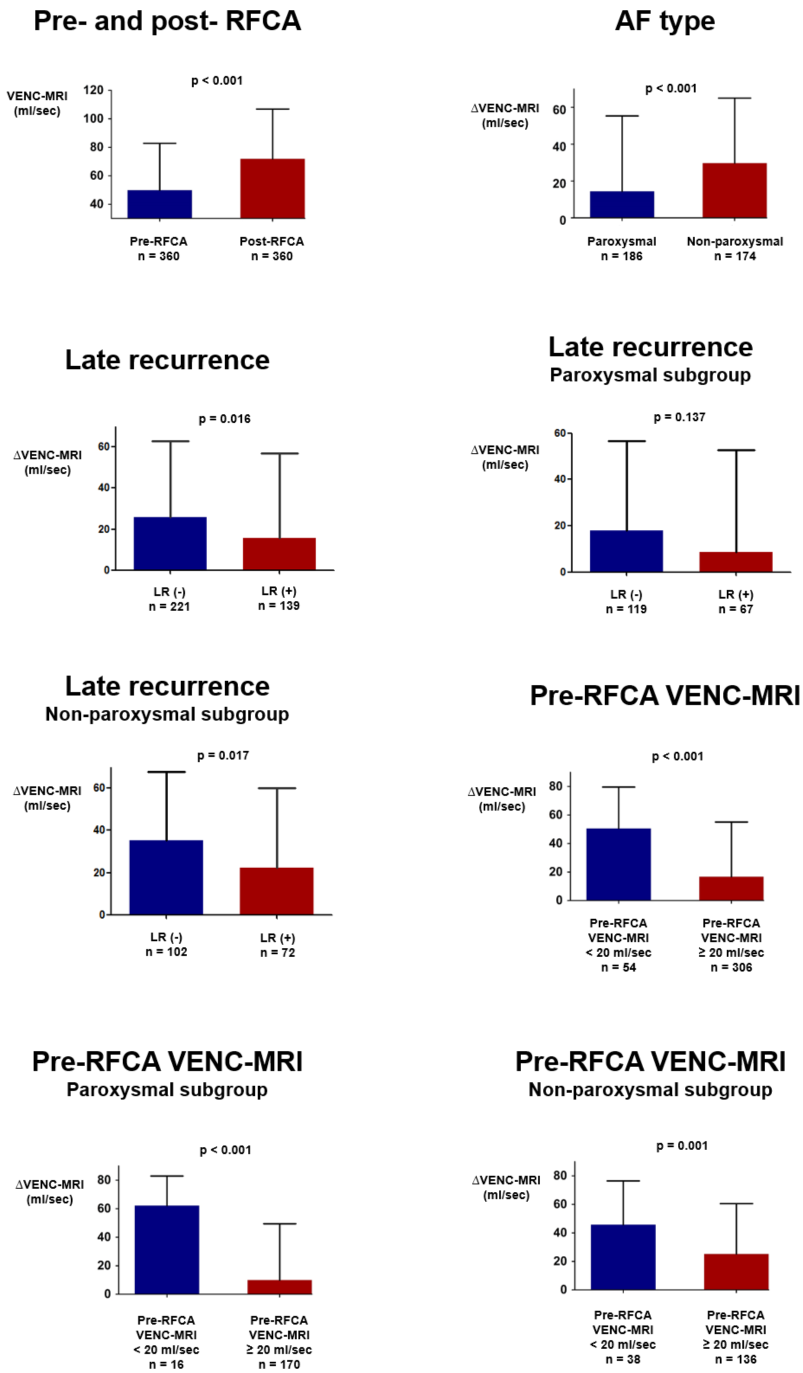


**Figure 2.** Impact of RFCA on VENC-MRI: univariate analysis.

RFCA was associated with significant improvement in VENC-MRI. Patients with non-paroxysmal AF and low pre-RFCA VENC-MRI had greater improvement in VENC-MRI. Late recurrence had negative impact on VENC-MRI.

AF: atrial fibrillation; RFCA: radiofrequency catheter ablation; VENC-MRI: velocity-encoded cardiac magnetic resonance imaging.

**Figure 3**

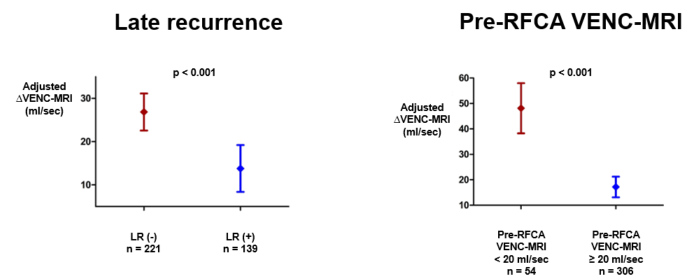


**Figure 3.** Impact of RFCA on VENC-MRI: multivariate analysis.

Late recurrence (adjusted for sex, AF type, and pre-RFCA VENC-MRI) and pre-RFCA VENC-MRI (adjusted for sex, AF type, and late recurrence) were significantly associated with [?]VENC-MRI after RFCA.

AF: atrial fibrillation; RFCA: radiofrequency catheter ablation; VENC-MRI: velocity-encoded cardiac magnetic resonance imaging.

**Table 1.** Baseline characteristics of the study population.

| | N = 360 |
|---|---|
| **Age (year)** | 57.31 ± 11.16 |
| **Sex (Male)** | 278 (77.2%) |
| **Body weight (kg)** | 71.64 ± 10.99 |
| **Height (cm)** | 168.98 ± 8.43 |
| **Body mass index (kg/m$^2$)** | 25.03 ± 2.92 |
| **Heart failure** | 43 (11.9%) |
| **Hypertension** | 151 (41.9%) |
| **Diabetes mellitus** | 28 (7.8%) |
| **History of ischemic stroke** | 35 (9.7%) |
| **Vascular disease** | 16 (4.4%) |
| **$CHA_2DS_2$-VASc** | 1.40 ± 1.27 |
| **Non-paroxysmal AF** | 174 (48.3%) |
| **LA diameter (mm)** | 41.67 ± 6.03 |
| **LV ejection fraction (%)** | 54.40 ± 5.82 |
| **E over e’** | 8.423 ± 3.14 |
| **LAA flow velocity (cm/sec)** | 46.92 ± 21.43 |
| **Dense SEC** | 5 (1.4%) |
| **Pre-RFCA VENC-MRI (ml/sec)** | 49.85 ± 32.97 |
| **Post-RFCA VENC-MRI (ml/sec)** | 71.92 ± 34.94 |

AF: atrial fibrillation; LA: left atrium; LAA: left atrial appendage; LV: left ventricle; MRI: magnetic resonance imaging; RFCA: radiofrequency catheter ablation; SEC: spontaneous echo-contrast; VENC: Velocity-encoded.

**Table 2.** Factors associated with [?]VENC-MRI.

| | Univariate analysis | Univariate analysis | Multivariate analysis | M |
|---|---|---|---|---|
| | **Unstandardized coefficient** | **p value** | **Unstandardized coefficient** | **p** |
| Late recurrence | -12.020 | 0.016 | -10.864 | < |
| Non-paroxysmal AF | 15.297 | < 0.001 | 1.088 | 0 |
| Sex | 11.568 | 0.018 | 5.226 | 0 |
| Age | 0.212 | 0.252 | | |
| Body mass index (kg/m$^2$) | 0.661 | 0.348 | | |
| LA diameter (mm) | 0.543 | 0.112 | | |
| LV ejection fraction (%) | -0.460 | 0.194 | | |
| E over e’ | 0.121 | 0.855 | | |
| LAA flow velocity (cm/sec) | -0.392 | < 0.001 | | |
| Pre-RFCA VENC-MRI (ml/sec) | -0.636 | < 0.001 | -0.628 | < |

AF: atrial fibrillation; LA: left atrium; LAA: left atrial appendage; LV: left ventricle; MRI: magnetic resonance imaging; RFCA: radiofrequency catheter ablation; VENC: Velocity-encoded.