Left Atrial Geometry and Outcome of Atrial Fibrillation Ablation: Results from the Multicenter LAGO-AF Study

Felipe Bisbal MD PhD FESC[1,2], Francisco Alarcón MSc[3], Angel Ferrero MD[4], Juan Jose González-Ferrer MD [2,5], Concepción Alonso MD [6], Marta Pachón MD [7], Helena Tizón MD [8], Pilar Cabanas-Grandío MD PhD [9], Manuel Sanchez MD [10], Eva Benito MD [3], Albert Teis MD [1], Ricardo Ruiz-Granell MD [4], Julián Pérez-Villacastín MD [2,5], Xavier Viñolas MD [6], Miguel Angel Arias MD [7], Ermengol Vallés MD [8], Enrique García-Campo MD [9], Ignacio Fernández-Lozano MD [10], Roger Villuendas MD [1], Lluís Mont MD PhD FESC FEHRA [3]*.

Clinical Trial Registration Information: NCT02373982
(http://clinicaltrials.gov/ct2/show/NCT02373982)

[1] Heart Institute (iCor), University Hospital Germans Trias i Pujol, Badalona; [2] CIBERCV, Instituto de Salud Carlos III, Madrid, Spain; [3] Atrial Fibrillation Unit (UFA), Hospital Clinic, Universitat de Barcelona, IDIBAPS, Barcelona; [4] Hospital Clinic de Valencia, Valencia; [5] Hospital Clinico San Carlos, Madrid; [6] Hospital de la Santa Creu i Sant Pau, Barcelona; [7] Hospital Virgen de la Salud, Toledo; [8] Hospital del Mar, Barcelona; [9] Hospital Álvaro Cunqueiro, Vigo; [10] Hospital Puerta de Hierro, Majadahonda, Spain

Conflict of interest: FB has served as a consultant for St. Jude Medical. LM has served as a consultant for Biosense-Webster, Boston Scientific, and St. Jude Medical.

Running title: Remodeling predictors of AF ablation outcome

Wordcount: 3474

*** Author for correspondence:**

Dr. Lluís Mont
Cardiology Department, Hospital Clinic
Villarroel 170, 08036-Barcelona
Tel: +3493-2275551; Fax: +34-93-4513045
lmont@clinic.cat

ABSTRACT

Introduction Left atrial (LA) remodeling is a key determinant of atrial fibrillation (AF) ablation outcome. Optimal methods to assess this process are scarce. LA sphericity is a shape-based parameter shown to be independently associated to procedural success. In a multicenter study, we aimed to test the feasibility of assessing LA sphericity and evaluate its capability to predict procedural outcomes.

Methods This study included consecutive patients undergoing first AF ablation during 2013. A 3D model of the LA chamber, excluding pulmonary veins and LA appendage, was used to quantify LA volume and sphericity (≥82.1% was considered spherical LA).

Results In total, 243 patients were included across 9 centers (71% men, aged 56±10 years, 44% with hypertension and 76% CHA_2DS_2-VASc≤1). Most patients had paroxysmal AF (66%) and underwent radiofrequency ablation (60%). Mean LA diameter, volume, and sphericity were 42±6mm, 100±33ml, and 82.6±3.5%, respectively. Adjusted Cox models identified paroxysmal AF (HR 0.54, p=0.032) and LA sphericity (HR 1.87, p=0.035) as independent predictors for AF recurrence. A combined clinical-imaging score (LAGO) including 5 items (AF phenotype, structural heart disease, CHA_2DS_2-VASc≤1, LA diameter and LA sphericity) classified patients at low (≤2 points) and high risk (≥3 points) of procedural failure (35% vs 82% recurrence at 3-year follow-up, respectively; HR 3.10, p<0.001).

Conclusion In this multicenter, real-life cohort, LA sphericity and AF phenotype were the strongest predictors of AF ablation outcome after adjustment for covariates. The LAGO score was easy to implement, identified high risk of procedural failure, and could help select optimal candidates.

KEYWORDS: Atrial Fibrillation, Ablation, Left Atrium, Remodeling, Sphericity, Magnetic Resonance, Cardiac Computed Tomography

CONDENSED ABSTRACT

In this multicenter, real-life cohort (243 patient, 9 centers) demonstrates LA sphericity (HR 1.87) and AF phenotype (HR 0.54) as the strongest predictors of AF ablation outcome after adjustment for covariates. A new clinical-imaging score (LAGO) identified high risk of procedural failure (HR 3.10), and could help select optimal candidates.

WHAT'S NEW?

- AF ablation success is highly dependent on atrial disease stage. Methods to assess LA remodeling are crucial to determine disease progression and help to select optimal candidates.
- LA sphericity is a shape-based remodeling parameter independent of size. In a single center MRI study was found to be associated to procedural success.
- The present study demonstrates, in a multicenter fashion, LA sphericity as the only imaging parameter with independent predictive value for recurrence after first AF ablation, after adjusting for covariates, regardless of AF phenotype, imaging modality, energy source, and center experience.
- We propose a simple clinical-imaging "LAGO" score that easily identified patients at high risk of procedural failure, and could be clinically useful to select optimal candidates for ablation.

INTRODUCTION

Ablation has become the cornerstone of treatment for symptomatic atrial fibrillation (AF).[1] However, patient outcomes differ significantly depending on clinical characteristics and AF phenotype.[2] Recent evidence supports that left atrial (LA) remodeling is the most important factor in procedural success.[3] Methods to assess LA remodeling have evolved substantially, allowing deeper characterization of this progressive disease. The use of M-mode LA diameter (LAD) as the standard to evaluate LA remodeling has been progressively abandoned.[4] Instead, 3D imaging modalities have been shown to better define chamber volumes and shape, the presence and extent of myocardial fibrosis, and, with speckle tracking, the functional status of the LA.[5–8] Most of these parameters, however, are confined to the research field.

Left atrial sphericity, defined as the variation between actual LA shape and a perfect sphere, was first described in a single center MRI study as a new shape-based remodeling parameter strongly and independently associated to procedural failure: the higher the LA sphericity, the higher the probability of recurrence.[8]

The aim of the study was to test the feasibility of assessment in a multicenter study (including different imaging modalities and ablation approaches) and to evaluate its capability to predict procedural outcomes.

METHODS

Study Design

This was a multicenter, observational study of a cohort of consecutive patients undergoing a first ablation procedure for paroxysmal and persistent AF. The main objective was to validate at multiple centers the predictive value of LA sphericity, assessed by 3D imaging, in the outcomes of AF ablation.

Study Population

The study included patients from January 1 to December 31, 2013, who underwent a first ablation of symptomatic drug-refractory paroxysmal and persistent AF. Three-dimensional imaging of the LA was acquired prior to the procedure with computed tomography (CTA) or magnetic resonance angiograms (MRA). Patients with previous catheter or surgical LA ablation were excluded.

Minimum requirements for participating centers included a minimum of 25 AF ablations/year, pulmonary vein isolation (PVI) as procedural endpoint (radiofrequency or cryoenergy), pre-procedural 3D imaging in at least 50% of procedures, and data collection on baseline, procedural, and follow-up variables of interest in prospective institutional databases. All patients must have given consent for their inclusion in institutional databases. Nine out of 16 centers screened met these criteria and participated in the study. Centers were categorized as high (≥100 AF ablations/year) or low (<100 AF ablations/year) volume according to previous literature.[9]

A dataset of 10 MRA of non-AF volunteers was analyzed to explore LA spherical deformation in young, healthy individuals. Details of this population were previously reported.[10]

The study protocol was approved by the hospitals' Ethics Committee.

3D image postprocessing

Each center applied institutional acquisition protocols for pre-procedural CTA or MRA; postprocessing, previously described in detail,[8] was centralized in a single center. In summary, a 3D reconstruction of LA cavity (CT and MR) was created with the CARTO 3® (Biosense Webster, Diamond Bar, CA, USA) image integration plug-in after excluding PVs and LA appendage at their ostia. The resulting 3D model was imported to ADAS-AF™ (Galgo Medical, Barcelona, Spain) to calculate remodeling values including LA volume (LAV) and sphericity. Quantification of LA remodeling parameters was blinded to clinical and ablation data.

Conceptually, LA sphericity quantifies the variation between the LA shape and a perfect sphere (Figure 1). Detailed mathematical formulae have been thoroughly specified in previous publications.[8] Briefly, LA sphericity is the coefficient of variation of the sphere (CVS), a non-dimensional parameter (independent of size) that captures the shape by dividing the standard deviation of the average radius (AR) of the sphere by the AR. The AR is calculated as the mean of distances between all points of the LA wall (3D model) and the center of the LA. To facilitate understanding of the value, it is expressed as a percentage: (1- CVS)*100.
The aim of the study was to test the validity of LA sphericity categories in an external, heterogeneous, real-life cohort. For this purpose, the same cutoff values of the seminal paper were used to define spherical categories: Group 1 ≤ 82.1% < Group 2 < 85.7% ≤ Group 3.

Ablation procedure

Ablation was performed according to institutional protocols for paroxysmal and persistent AF, which included both contact and non-contact force sensing catheters, as well as first and second generation cryoballoon technologies. All centers using point-by-point radiofrequency ablation reported using wide antral circular ablation to achieve PVI.

All patients underwent pre- and postprocedural oral anticoagulation (international normalized ratio between 2 and 3) for at least 1 month before and after ablation. As a general rule, antiarrhythmic drugs (AAD) were discontinued ≥5 half-lives before ablation (or ≥1 week for amiodarone). In the majority of cases, transesophageal echocardiography was performed before ablation to exclude the presence of LA thrombus. After transseptal puncture, a bolus of i.v. heparin was administered according to patient weight, followed by additional boluses/continuous infusion to maintain an activated clotting time of 250-350 seconds.

Radiofrequency ablation began with a 3D map using an electroanatomic mapping system (CARTO, Biosense Webster, Diamond Bar, CA, USA or Ensite, St Jude Corporation, St Paul, MN, USA). In some cases, CTA or MRA were integrated into the navigation system to improve LA anatomic reconstruction. Wide encircling pulmonary vein ablation was performed using radiofrequency energy (open-irrigated tip catheter) assisted by a circular multipolar catheter. Additional ablation lines or ablation of complex fractioned electrograms were performed according to each hospital's protocol.

For cryoballoon ablation, an inner-lumen mapping catheter (Achieve™, Medtronic¸ Minneapolis, MN, USA) was advanced to each PV ostium through a steerable 15 Fr sheath (FlexCath Advance™, Medtronic) to monitor PV potentials. A 28-mm Cryoballoon (Arctic Front or Arctic Front Advance™, Medtronic) was advanced, inflated, and positioned at each PV ostium until optimal occlusion was achieved. Cryoenergy was then delivered up to 240 seconds to achieve PVI, applying a bonus freeze as a general rule. Cryoenergy at right-side pulmonary veins was applied under phrenic nerve monitoring by pacing at superior vena cava.

Post-ablation management and follow-up

Treatment with AAD during the first 3 months after ablation was prescribed according to physician preference. As a general rule, class IC drugs were first choice in patients with no structural heart disease and paroxysmal AF; class III were preferred in cases of structural heart disease or persistent AF. Continuation of AAD therapy beyond 3 months post-ablation was based on documented AF recurrence or symptoms without any documented atrial arrhythmia.

Patient follow-up included a minimum of 3 visits at the outpatient clinic (3, 6 and 12 months post-ablation) with 12-lead ECG and at least one 24-hour Holter monitoring. When available, a more prolonged rhythm monitoring was performed with 2-, 3- or 7-day Holter or implantable loop recorder (ILR, Reveal XT, Medtronic, MN). Between scheduled visits, patients were instructed to seek medical care, to include an ECG whenever they presented with symptoms.

Primary endpoint was defined as any documented AF or flutter lasting more than 30 seconds by ECG, Holter or ILR during follow-up. No blanking period was considered after the ablation procedure.

Statistical Analysis

Continuous data are expressed as mean±SD, median, and interquartile range (IQR) or number (percentage) as appropriate. The $\chi 2$ or Fisher exact test was used to compare proportions between groups. Student t, Mann–Whitney U, one factor ANOVA, or Kruskal-Wallis tests were used to compare continuous variables between groups according to normality assumptions. Survival analysis using Cox proportional hazards model was used to identify univariate and multivariate predictors of AF recurrence after first AF ablation. A P-value of ≤0.05 was considered significant. Analysis was performed using SPSS 19.0 statistical package (SPSS, Chicago, IL, USA).

RESULTS

In total, 473 patients underwent AF ablation at the 9 participating centers in 2013. Three centers were categorized as high volume (33%). Patients undergoing repeat AF ablation, those with no or suboptimal pre-procedural imaging or with inadequate follow-up were excluded. A final cohort of 243 patients was included in the final dataset (Supplemental figure S1). Most patients had paroxysmal AF (66%) and low CHA_2DS_2-VASc scores (≤1 in 67%). Ablation was performed a median of 43 (24-72) months after AF diagnosis and radiofrequency was the most common energy source used for ablation (60%). There were 14 non-fatal complications (5.7%), due to vascular access complications (4), cardiac tamponades (3), pericarditis (3), and transient ischemic attack, phrenic nerve palsy, acute pulmonary edema, and hemoptysis (1 each). There were no deaths. Detailed baseline and procedural characteristics are listed in Table 1.
After a median (IQR) follow-up of 457 (351-764) days, the overall recurrence rate after first procedure was 43.3%, occurring after a median (IQR) of 182 (92-367) days. Considering a 3-month blanking period, the recurrence rate dropped to 34.8%, with a median (IQR) time-to-recurrence of 305 (179-468) days (Supplemental figure S2). Three quarters of the patients received AAD during the first 3 months after ablation (class I in 63% of cases), and 39% of all patients received ongoing treatment (class I in 55% of cases). Repeat AF ablation was required in 17% of patients.

Post-ablation rhythm monitoring was performed with 24-hour Holter in the majority of cases (72%). Longer monitoring was performed in 26%, including 2, 3, and 7-day Holter recordings and implantable loop recorders. Only 3 patients (1.2%) were monitored with ECG-only.

Left Atrial Remodeling

3D imaging was obtained with MRA in most cases (61%). Measurements of LA remodeling are detailed in Table 2. Mean LA sphericity was 82.6 ± 3.5% and most patients (59%) showed spherical deformation (including groups 2 and 3). Healthy controls showed significantly lower mean LA sphericity and LAV (76.50±3.21 and 34.4±8.6ml, respectively; $p<0.001$).

LA sphericity was weakly but significantly correlated with LAD ($R=0.342$; $p<0.01$) and LAV ($R=0.327$; $p<0.001$). Important collinearity was observed between LA sphericity and both LAD and LAV (eigenvalue of 0.001 and condition index 48).

Probability of recurrence after first procedure was greater in patients with spherical LA (groups 2 and 3) compared to those with discoid LA (group 1) after one (38% vs 25%), two (58% vs 44%) and three (73% vs 47%) years of follow up (log rank $p=0.026$) (Figure 2).

Patients with spherical LA had higher BMI and more dilated LA, and more often received ablation in high-volume centers (Table 3). Paradoxically, patients with a more spherical atrium had a lower proportion of high blood pressure and prior CV. It is noteworthy that AF phenotype and AF duration did not differ between LA sphericity groups, and no differences were observed in AAD use, cardioversion, or repeat ablation during follow-up. There was a higher proportion of non-paroxysmal AF in patients with dilated LA (43.3% vs 22.0% assessed by LAD, $p=0.002$ and 42.3% vs 26.9% assessed by LAV, $p=0.012$).

Predictors of Ablation Outcome

Univariate Cox regression analysis identified significant associations between adverse outcome after AF ablation and persistent AF, radiofrequency ablation, spherical LA, and dilated LA, whether assessed by LAD or volume. A trend toward increased risk of recurrence in patients with structural heart disease was also observed. Detailed description is provided in Supplemental Table S1.

Multivariate Cox proportional hazard analysis was performed to identify independent risk factors for recurrence (Table 4). Seven variables with significant association in the univariate Cox models and other previously reported independent predictors were included: high-volume centers, obesity, structural heart disease, CHA_2DS_2-VASc ≤1, AF phenotype, time since AF diagnosis, and energy source. Due to serious collinearity problems, five separate models were tested: LA sphericity (model 1), LAV (model 2), LAD (model 3), both LA sphericity and LAD (model 4) and LA sphericity, LAV, and LAD (model 5).

Paroxysmal AF and spherical remodeling were the only factors independently associated with recurrence across all models (HR ≈ 0.5 and HR ≈ 2, respectively). CHA_2DS_2-VASc (≤1) showed independent predictive value with a HR ≈ 0.5 when LAD was not included (models 1 and 2). Presence of structural heart disease remained significant only in model 1 (HR ≈ 2).

LA dilation assessed by LAD was found to be independently associated with recurrence. When LA sphericity was included in the model, however, the significance did not persist. Remarkably, LAV was not associated with recurrence when adjusted for other covariates.

New Scoring System to Predict Recurrences

A new clinical- and imaging-based model for pre-procedural risk stratification (Left Atrial Geometry and Outcome [LAGO] score) was built upon the identified predictors of recurrence: AF phenotype, presence of structural heart disease, CHA_2DS_2-VASc ≤1, dilated LA, and spherical LA (scoring 1 point each). The area under the curve was 0.687 (95% CI 0.610-0.765; p<0.001). Cutoff point of 3 (LR+ of 3; sensitivity 21%, specificity 94%) was independently associated with recurrence (HR 3.10 [95% CI 1.94-4.95]; p<0.001) (Figure 3). Patients scoring ≤2 had better short- and mid-term outcome compared to those with ≥3 points (probability of recurrence of 22% vs 50% at 1 year and 35% vs 82% at 3 years of follow-up).

DISCUSSION

To our knowledge, this is the first study to validate the value of LA sphericity in predicting AF ablation outcome in a multicenter cohort. The study had 3 main findings: 1) LA sphericity was the only remodeling parameter with independent predictive value for AF ablation outcome regardless of AF phenotype, energy source, imaging modality, and operator experience; 2) Persistent AF was the only clinical factor associated with recurrences after adjustment for covariates; 3) A 5-item scoring system including clinical and imaging parameters better identified patients at very high risk of recurrence at mid-term follow-up.

LA remodeling in AF

Remodeling of the LA is the final pathway of a high number of cardiac diseases. Any condition generating volume or pressure overload of the LA could be considered a causal factor for AF development. In addition, AF itself promotes electrical, tissue, and structural changes of the LA, which promote the perpetuation of the arrhythmia (“AF begets AF”).[11]

Structural remodeling has been classically defined as LA enlargement: both diameter and volume are increased in patients with AF, compared to those in sinus rhythm.[12] However, although LA size (especially volume) was a strong predictor of cardiovascular outcomes in patients in sinus rhythm, the predictive value in patients with AF was poor.[12]

The present study is the first to also provide LA shape analysis of a young, healthy population, allowing an approximation to normality of spherical deformation. As with size, LA sphericity was increased in patients with diagnosed AF, compared to healthy controls in sinus rhythm. However, conclusions on the impact of AF in spherical deformation cannot be drawn from this analysis. Further comparison adjusted for covariates is warranted.

In our previous work,[8] LA sphericity was shown to be associated with risk factors such as hypertension, sleep apnea, and presence of structural heart disease, as well as AF phenotype (higher sphericity in patients with non-paroxysmal AF). In another study, LA sphericity was strongly associated with thromboembolic events in patients with AF, compared to controls: the higher the spherical deformation the greater the likelihood of stroke.[13]

In our cohort, all imaging parameters of LA remodeling were mildly but significantly correlated. It is noteworthy that AF phenotype was correlated with LA dilation but not with spherical deformation. This finding was confirmed in multivariate models, as both AF phenotype and LA sphericity were independently associated with recurrence. Similar findings with LA fibrosis were observed in the multicenter DECAAF study,[7] suggesting that degree of atrial remodeling is not necessarily related to a particular AF pattern. Although indication and predicted outcome for AF ablation is usually based on AF phenotype, the findings of our study and those of Marrouche *et al* encourage a more refined assessment of LA disease before deciding the best therapeutic strategy for each patient.

AF Ablation Outcome

Current guidelines recommend LA size quantification to assess the remodeling process associated with AF.[1] In patients suitable for ablation due to symptomatic drug-refractory AF, an association between LA dilation and worse outcome has been suggested; however, due to the weakness of the evidence, current guidelines do not state any recommendation on patients' suitability for ablation in terms of LA size.[1] A recent meta-analysis evaluating individual baseline clinical and remodeling characteristics failed to find an association between LA size and recurrences.[14] Better characterization of the remodeling process associated with AF beyond size is therefore needed to improve ablation results. Evidence on more refined LA structural and functional parameters is growing and demonstrates strong association with the likelihood of procedural success.[6,7,15,16]

In this regard, previous single center series (106 patients) showed spherical deformation of the LA to be independently associated with the probability of recurrence after last AF ablation (mean of 1.4 procedures/patient).[8] The main limitations of our previous series were the bias of a single, high-volume center with very experienced operators; single imaging modality (MRA); and not accounting for current state-of-the-art ablation tools (only radiofrequency without contact-force sensing was used). The present study was designed to overcome these limitations and test 3D-imaging remodeling predictors of AF ablation outcome after a first procedure in a multicenter cohort, including a wide spectrum of center profiles (low vs high volume, experienced vs less-experienced operators), different energy sources (cryoballoon vs radiofrequency), and different imaging modalities (CT and MRI) to emulate real-life clinical practice. Demonstration of the independent predictive value of LA sphericity in this setting represents a clinically meaningful finding, providing strong evidence of its applicability in a wide range of clinical settings.

Although LA size and recurrence were associated in univariate Cox analyses, both diameter and volume were rendered nonsignificant when adjusted for covariates. These findings mimic our previous report and those from Marrouche et al, suggesting that more advanced imaging characterization tools (LA sphericity or fibrosis) may be superior to size quantification alone for the precise definition of LA disease progression, and may better stratify risk of recurrence.

Contrary to previous reports,[17] the volume of AF ablation procedures per center/year did not impact outcome.

Risk Prediction Scheme

LAGO score is a simple risk prediction model that combines five clinical and imaging variables, each of which provides additive predictive value for AF recurrence. This allows easy identification of patients with high scores (≥3 points) who are unlikely to remain in sinus rhythm at 3-year follow-up (<15% likelihood), and for whom ablation should not be advised as a rhythm control strategy.

Limitations

The main limitation of the study is its retrospective nature; nevertheless, the baseline, procedural and follow-up data were extracted from prospective institutional databases. Image acquisition and ablation approach protocols were not homogeneous across centers. In our view, this constitutes a strength rather than a weakness of the study, as the results reflect the heterogeneous, real-life cases encountered in daily practice and confirms, to some extent, the broad applicability of LA sphericity.

Exclusion of patients due to incomplete baseline or follow-up data could introduce a selection bias; however, these exclusions were mostly driven by incomplete pre-procedural evaluation and follow-up from the referral physicians and was not necessarily related to specific patient profiles.

CONCLUSION

In this multicenter study, LA sphericity was the only imaging parameter with independent predictive value for recurrence after first AF ablation, after adjusting for covariates, regardless of AF phenotype, imaging modality, energy source, and center experience. The simple clinical-imaging “LAGO” score easily identified patients at high risk of procedural failure, and could be clinically useful to select optimal candidates for ablation.

ACKNOWLEDGMENTS

This study was funded by CIBER Cardiovascular (CB16/11/00403), Red de Investigación Cardiovascular (RD12/0042/0047), and La MARATO - TV3 (ID 201527).

REFERENCES

1. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Europace* 2016;18:1609–1678.

2. Balk EM, Garlitski ACNNC, Alsheikh-Ali A a, Terasawa T, Chung MEI, Ip S. Predictors of atrial fibrillation recurrence after radiofrequency catheter ablation: a systematic review. *J Cardiovasc Electrophysiol* 2010;21:1208–1216.

3. O'Neill L, Harrison J, O'Neill M, Williams SE. Clinical, electrophysiological and imaging predictors of atrial fibrillation ablation outcome. *Expert Rev Cardiovasc Ther* 2017;15:289–305.

4. Lang RM, Badano LP, Mor-avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults : An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;28:1–39.e14.

5. Sohns C, Sohns JM, Vollmann D, Lüthje L, Bergau L, Dorenkamp M, et al. Left atrial volumetry from routine diagnostic work up prior to pulmonary vein ablation is a good predictor of freedom from atrial fibrillation. *Eur Heart J Cardiovasc Imaging*. 2013;14:684–691.

6. Montserrat S, Gabrielli L, Bijnens B, Borràs R, Berruezo A, Poyatos S, et al. Left atrial deformation predicts success of first and second percutaneous atrial fibrillation ablation. *Heart Rhythm* 2015;12:11–8.

7. Marrouche NF, Wilber D, Hindricks G, Jais P, Akoum N, Marchlinski F, et al. Association of atrial tissue fibrosis identified by delayed enhancement MRI and atrial fibrillation catheter ablation: the DECAAF study. *JAMA* 2014;311:498–506.

8. Bisbal F, Guiu E, Calvo N, Marin D, Berruezo A, Arbelo E, et al. Left atrial sphericity: A new method to assess atrial remodeling. impact on the outcome of atrial fibrillation ablation. *J Cardiovasc Electrophysiol* 2013;24:752–759.

9. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, et al. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circ Arrhythm Electrophysiol* 2010;3:32–38.

10. Benito EM, Carlosena-remirez A, Guasch E, Perea RJ, Figueras R, Borras R, et al. Left atrial fibrosis quantification by late gadolinium-enhanced magnetic resonance : a new method to standardize the thresholds for reproducibility. Europace 2016 Dec 8. pii: euw219 [Epub ahead of print].

11. Allessie M, Ausma J, Schotten U. Electrical, contractile and structural remodeling during atrial fibrillation. *Cardiovasc Res* 2002;54:230–246.

12. Tsang TSM, Abhayaratna WP, Barnes ME, Miyasaka Y, Gersh BJ, L DPHI, et al. Prediction of cardiovascular outcomes with left atrial size: is volume superior to area or diameter? *J Am Coll Cardiol* 2006;47:1018–1023.

13. Bisbal F, Gomez-pulido F, Cabanas-GrandÍo P, Akoum N, Calvo M, Andreu D, et al. Left Atrial Geometry Improves Risk Prediction of Thromboembolic Events in Patients With Atrial Fibrillation. *J Cardiovasc Electrophysiol* 2016;27:804–810.

14. Balk EM, Garlitski ACNNC, Alsheikh-Ali A a, Terasawa T, Chung MEI, Ip S. Predictors of atrial fibrillation recurrence after radiofrequency catheter ablation: a systematic review. *J Cardiovasc Electrophysiol* 2010;21:1208–1216.

15. Habibi M, Lima JAC, Khurram IM, Zimmerman SL, Zipunnikov V, Fukumoto K, et al. Association of left atrial function and left atrial enhancement in patients with atrial fibrillation cardiac magnetic resonance study. *Circ Cardiovasc Imaging* 2015 Feb;8(2):e002769.

16. Bax JJ, Marsan NA, Delgado V. Non-invasive imaging in atrial fibrillation: focus on prognosis and catheter ablation. *Heart* 2015;101:94–100.

17. Deshmukh A, Patel NJ, Pant S, Shah N, Chothani A, Mehta K, et al. In-hospital complications associated with catheter ablation of atrial fibrillation in the United States between 2000 and 2010: Analysis of 93 801 procedures. *Circulation*. 2013;128:2104–2112.

FIGURE LEGENDS

Figure 1. Left atrial sphericity (LASP) categories: examples of discoid (A) and spherical-shaped LA (B) corresponding to low and high LASP, respectively. Posterior and right lateral views of 3D model are displayed. LAV, LA volume.

Figure 2. Kaplan-Meier plot for AF-free survival by LA sphericity

Figure 3. Kaplan Meier plot for AF-free survival by LAGO score (non-adjusted). Patients scoring ≤2 had better outcome than those with higher scores (35% vs 82% recurrence at 3-year follow-up).

Table 1. Baseline, procedural and follow-up patient characteristics

	Mean ±SD / %
Age	56.6 ± 9.7
Sex (Male)	71.0 %
BMI	27.8 ± 4.4
Obesity (BMI >30)	27.8%
HBP	107 ± 44.4
DM	8.7 %
SOAS	8.7 %
SHD	16.3 %
LVEF	61.5 ± 10.6
Prior stroke	3.3 %
CHA_2DS_2-VASc (mean)	1.21 ± 1.17
0	32.6 %
1	34.3 %
2	18.8 %
3	9.2 %
4	4.6 %
≥5	0.4 %
CHA_2DS_2-VASc ≤1	66.9 %

	Mean ±SD / %
Paroxysmal AF	66.0 %
AF duration (months)	43 ± 48
Prior CV	27.8 %
Energy source (RF)	60.3 %
Ablation time (min)	33.3 ± 16.4
PVI check	98.8 %
Substrate ablation	7.1 %
Procedural time (min)	190.6 ± 57.9
Fluoroscopy time (min)	32.7 ± 26.7
Complications	6.2 %
AAD blanking	75.5 %
Class I	63.4 %
Class III	35.0 %
Class I+III	1.6 %
AAD post-blanking	38.6 %
Class I	54.8 %
Class III	44.1 %
Class I+III	1.1 %
CV follow-up	9.2 %
Repeat AF ablation	17.1 %
Follow-up Holter 24h	72.4 %
Follow-up Holter ≥ 48h	26.4 %
Follow-up ECG only	1.3 %

Abbreviations: AF, atrial fibrillation; AAD, antiarrhythmic drug; BMI, body mass index; CV, cardioversion; DM, diabetes mellitus; HBP, high blood pressure; LVEF, left ventricular ejection fraction; PVI, pulmonary vein isolation; RF, radiofrequency; SOAS, sleep obstructive apnea syndrome; SHD, structural heart disease.

Table 2. Left atrial remodeling parameters

		Mean (SD) / %
LAD (mm)		41.5 ± 5.9
Dilated LA (by LAD)		43 %
LAV		99.6 ± 33.4
Dilated LA (by LAV)		46.1 %
Indexed LAV		50.9 ± 16.4
LA sphericity		82.62 ± 3.51
	Group 1	40.7 %
	Group 2	39.8 %
	Group 3	19.5 %
Spherical LA		59.3 %

Abbreviations: LA, left atrium; LAD, left atrial diameter; LAV, left atrial volume

Table 3. Baseline, procedural, and imaging characteristics, by LA sphericity group

	DISCOID LA Mean ± SD / %	**SPHERICAL LA** Mean ± SD / %	***P* value**
Age	56.4 ± 8,6	56.7 ± 10.5	0.786
Sex (Male)	72.4%	69.9%	0.672
BMI	**26.9 ± 4.0**	**28.5 ± 4.6**	**0.015***
Obesity	23.4%	31.3%	0.244
HBP	**52%**	**39.2%**	**0.048***
SOAS	10%	7.7%	0.497
SHD	14.3%	17.7%	0.478
LVEF	61.1 ± 11.5	62.0 ± 9.1	0.533
CHA_2DS_2-VASc **	1 (0-2)	1 (0-2)	0.712
CHA_2DS_2-VASc 0	30.1%	33.8%	0.642
CHA_2DS_2-VASc ≤1	67.0%	66.9%	0.986
Paroxysmal AF	70.4%	62.9%	0.229
AF Time	56.3 ± 46.0	51.7 ± 41.1	0.433
Prior CV	**35.7%**	**23.0%**	**0.033***
High-volume center	**50%**	**69.2%**	**0.003***
RF time	32.1 ± 13.5	34.3 ± 18.5	0.487
Substrate ablation	5.1%	8.4%	0.327
CV follow-up	6.1%	11.3%	0.175
Repeat ablation	13.3%	19.7%	0.192
AAD post-blanking	28.1%	33.8%	0.356
LA sphericity	**79.24 ± 2.49**	**84.94 ± 1.84**	**<0.001***
LA diameter	**39.5 ± 5.7**	**42.7 ± 5.7**	**<0.001***
Dilated LA (by LA diameter)	**42.1%**	**60.5%**	**0.012***
LA volume	**92.6 ± 28.4**	**104.4 ± 35.7**	**0.007***
Dilated LA (by LA volume)	**34.7%**	**53.8%**	**0.003***
Indexed LA volume	**47.9 ± 14.7**	**53.2 ± 17.4**	**0.034***

Abbreviations as in table 1 and 2. * Statistically significant, **U Mann-Whitney Test

Table 4. Multivariate Cox proportional hazard models for prediction of recurrences after AF ablation.

	MULTIVARIATE COX REGRESSION									
	MODEL 1		MODEL 2		MODEL 3		MODEL 4		MODEL 5	
	HR (95% CI)	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
High-volume center	0.91 (0.52-1.58)	0.740	0.80 (0.47-1.38)	0.424	0.85 (0.46-1.57)	0.601	0.92 (0.50-1.70)	0.796	0.90 (0.49-1.66)	0.728
Obesity	1.08 (0.64-1.84)	0.767	1.03 (0.61-1.75)	0.910	1.24 (0.68-2.28)	0.486	1.18 (0.65-2.14)	0.595	1.21 (0.66-2.23)	0.534
SHD	**2.06 (1.09-3.88)**	**0.026**	1.75 (0.93-3.27)	0.082	1.36 (0.66-2.79)	0.402	1.69 (0.82-3.46)	0.155	1.63 (0.79-3.37)	0.188
CHA_2DS_2-VASc ≤1	**0.54 (0.32-0.92)**	**0.024**	**0.55 (0.32-0.94)**	**0.029**	0.58 (0.33-1.02)	0.059	0.61 (0.35-1.07)	0.083	0.59 (0.33-1.03)	0.065
Paroxysmal AF	**0.51 (0.31-0.84)**	**0.008**	**0.56 (0.34-0.92)**	**0.021**	**0.52 (0.30-0.90)**	**0.020**	**0.51 (0.29-0.89)**	**0.018**	**0.54 (0.30-0.95)**	**0.032**
AF Time	1.00 (1.00-1.01)	0.699	1.00 (1.00-1.01)	0.730	1.00 (0.99-1.01)	0.699	1.00 (0.99-1.01)	0.937	1.00 (0.99-1.01)	0.978
Energy Source (RF)	1.47 (0.81-2.65)	0.202	1.33 (0.74-2.41)	0.342	1.06 (0.54-2.07)	0.867	1.16 (0.58-2.23)	0.676	1.13 (0.57-2.24)	0.725
Spherical LA	**1.85 (1.12-3.05)**	**0.017**					**1.92 (1.08-3.41)**	**0.026**	**1.87 (1.05-3.33)**	**0.035**
Dilated LA (LAV>100ml)			1.30 (0.78-2.17)	0.311					1.35 (0.74-2.32)	0.360
Dilated LA (LAD>42mm)					1.80 (0.98-3.31)	0.058	1.70 (0.92-3.17)	0.088	1.66 (0.88-3.11)	0.116

Abbreviations as in table 1 and 2.

Figure 1.

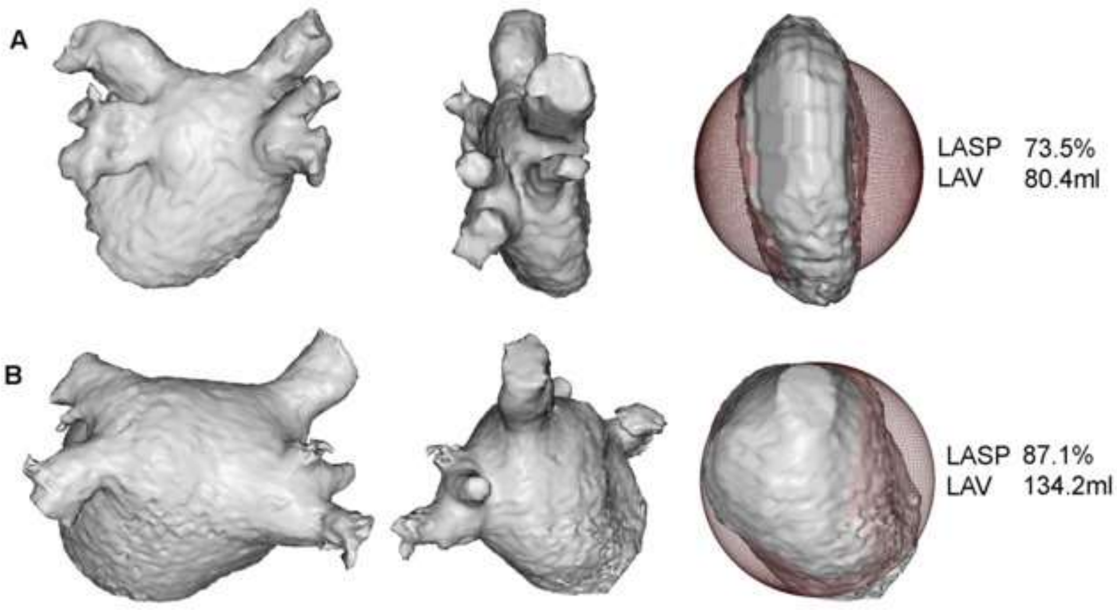
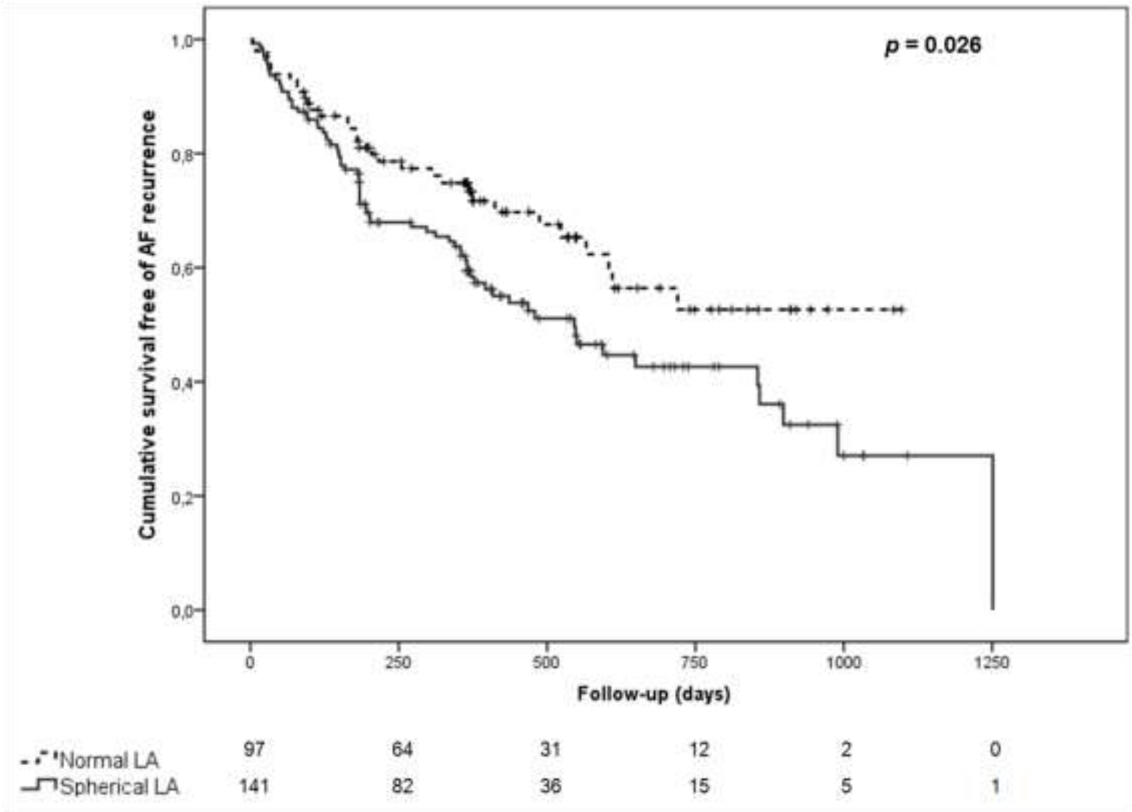
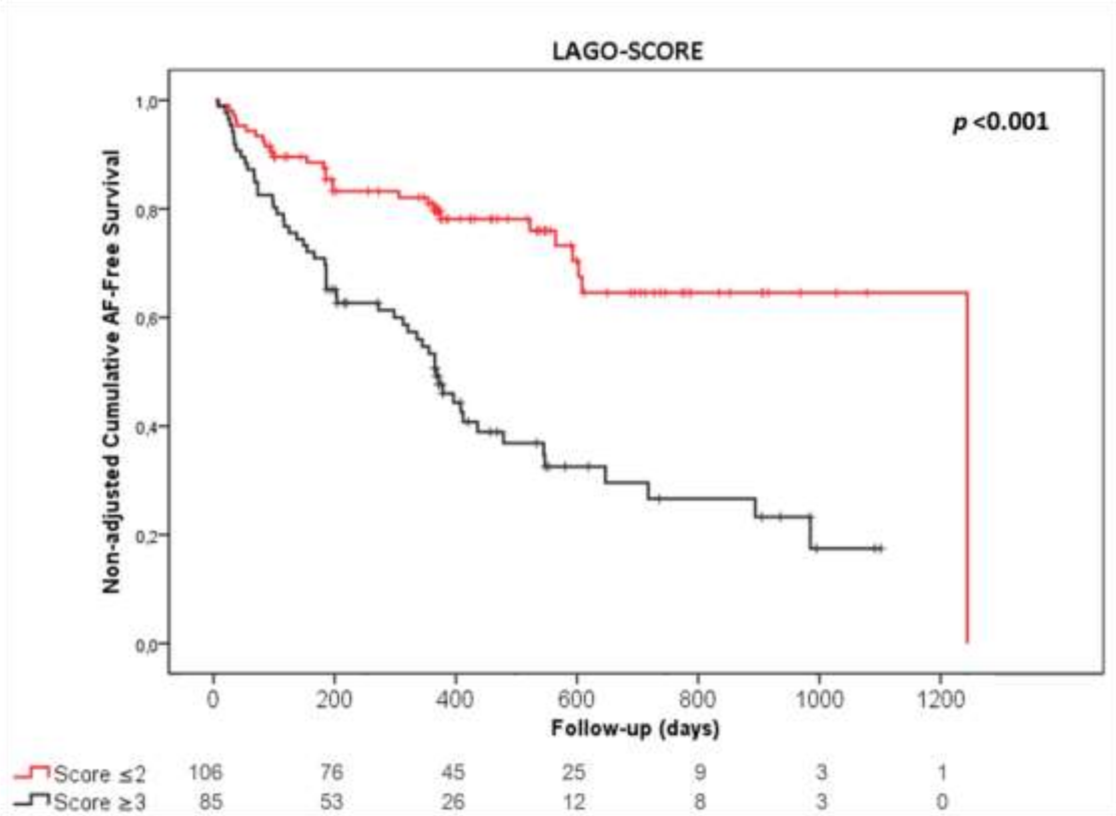


Figure 2


p = 0.026
Cumulative survival free of AF recurrence
1,0
0,8
0,6
0,4
0,2
0,0
0
250
500
750
1000
1250
Follow-up (days)
Normal LA 97 64 31 12 2 0
Spherical LA 141 82 36 15 5 1

438 Figure 3



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