

Low voltage in small left atrium in patients with persistent atrial fibrillation: left atrium diameter alone is not always a predictor of prognosis

Xiaoqin Li¹, Chun Yin¹, Yuan Zhang¹, Hao Zhang¹, Xiaoli Li¹, Wenli Wu¹, Boli Ran¹, YongJing Xiang¹, and Biao Fu¹

¹Chongqing Zhongshan Hospital

March 9, 2023

Abstract

Background The diameter of the left atrium (LA) is a major index of prediction for LA fibrosis and ablation outcome in atrial fibrillation (AF). However, an unenlarged LA may not be associated with good results in some cases of AF ablation. **Objective** Exploring the characteristics and ablation prognosis of the patients with fibrotic but unenlarged LA. **Methods** Patients with persistent fibrillation who underwent catheter ablation in our center were analyzed in this retrospective study. Comprehensive low voltage mapped in LA is considered a fibrotic LA. The patients with fibrotic but unenlarged LA, normal LA, and fibrotic tissue with enlarged LA were included in Groups A, B, and C, respectively. We compared clinical features, electrophysiological findings, immediate ablation results, and follow-up outcomes in three groups. **Results** We enrolled 9 patients in Group A, 38 in Group B, and 12 in Group C. There were greater proportions of women, low ventricular rates, and high CHA₂DS₂-VASC scores in the patients with fibrotic LA (Groups A and C). At the end of procedure, all of the patients saw restored sinus rhythm, and the rate of sinus rhythm was lower in Groups A and C than in Group B. Atrial-ventricular block and very-early-stage recurrence were more common in Group A. Sinus rhythm maintenance and LA reversion were rarer in Group A than in Group B or C. **Conclusions** A fibrotic but unenlarged LA was more likely to be seen in female with high CHADS₂VA₂S score. It indicated a poor prognosis for AF ablation.

Low voltage in small left atrium in patients with persistent atrial fibrillation: left atrium diameter alone is not always a predictor of prognosis

Low voltage in small left atrium in atrial fibrillation

Xiaoqin Li, MD,^a Chun Yin, MD,^a Yuan Zhang, MD,^a Hao Zhang, MD,^a Xiaoli Li, MD,^a Wenli Wu, MD,^a Boli Ran, MD,^a YongJing Xiang, RN,^a Biao Fu, MD,^a

From the ^aDepartment of Cardiology, Chongqing Zhongshan Hospital

Address for correspondence: Biao Fu, MD

Chongqing Zhongshan Hospital

312 Zhongshan First Road, Yuzhong District, Chongqing, China 401120.

Tel: 862363390551, e-mail: fbytt@qq.com.

Conflict of interest: none declared.

Total word count: 2500

Abstract

Background

The diameter of the left atrium (LA) is a major index for the prediction of LA fibrosis and ablation outcome in atrial fibrillation (AF). However, an unenlarged LA may not be associated with good results in some cases of AF ablation.

Objective

Exploring the characteristics and ablation prognosis of patients with fibrotic but unenlarged LA

Methods

Patients with persistent fibrillation who underwent catheter ablation in our center were analyzed in this retrospective study; comprehensive low voltage mapped in the LA was considered a fibrotic LA. The patients with fibrotic but unenlarged LA, normal LA, and fibrotic tissue with enlarged LA were included in Groups A, B, and C, respectively. We compared Clinical features, electrophysiological findings, immediate ablation results, and follow-up outcomes were compared among the three groups.

Results

We enrolled 9 patients in Group A, 38 in Group B, and 12 in Group C. There were greater proportions of women, low ventricular rates, and high CHA₂DS₂-VASC scores in the patients with fibrotic LA (Groups A and C). At the end of procedure, all of the patients saw restored sinus rhythm, and the rate of sinus rhythm was lower in Groups A and C than in Group B. Atrial-ventricular block and very-early-stage recurrence were more common in Group A. Sinus rhythm maintenance and LA reversion were rarer in Group A than in Group B or C.

Conclusions

A fibrotic but unenlarged LA was more likely to be observed in female with a high CHADS₂VA₂S score, indicating a poor prognosis for AF ablation.

Key words: atrial fibrillation fibrosis left atrium size ablation low voltage

Introduction

In patients with atrial fibrillation (AF), a long AF can cause enlargement of the left atrium (LA), which may progress to LA fibrosis, giving further poor prognosis for AF ablation (1-3). Enlarged LA alone could be considered an indication for AF fibrosis (4,5). However, we found that even some patients without enlarged LA showed comprehensive fibrosis during mapping and poor maintenance of sinus rhythm during follow-up. We analyzed these patients to determine their clinical features and develop a method for better prediction of outcome before AF ablation.

Methods

This was a retrospective study. We analyzed patients with persistent fibrillation (PeAF) who underwent catheter ablation at our center from January 2020 to January 2022. LA fibrosis was defined as comprehensive low voltage and iso-potentials (lack of high-frequency or fragmental potentials) mapped in both the left atrial and pulmonary veins (PV) in a 3D electro-anatomical system (Figure 1). The threshold of low voltage in LA was set to a cutoff < 0.35 mV, which was shown to be compatible with delayed-enhancement magnetic resonance imaging (MRI) detection of atrial fibrosis (6,7). We defined a small LA as any LA with a diameter of LA no more than 40 mm as evaluated by both ultrasound and CT. Patients with any prior history of AF ablation or moderate or severe mitral stenosis were excluded.

Patients with small LA and fibrosis were placed in Group A. We matched two groups of patients with persistent AF who underwent catheter ablation in the same period; one group contained patients with small LA but no LA fibrosis (Group B); the other group contained patients with large-diameter LA (40–50 mm) and LA fibrosis (Group C). Patients with LA larger than 50 mm were not analyzed, and their clinical characteristics, electrophysiological findings, and prognosis were compared.

The present study was performed in accordance with the Declaration of Helsinki (2000) and was approved and supervised by the Ethics Committee of Chongqing General Hospital. All patients provided full explanations of the procedures, and written informed consent was obtained from all patients.

Ablation procedure

A multipolar electrode catheter was deployed in the coronary sinus (CS), three-dimensional electroanatomic mapping was performed using CARTO3 (Biosense Webster, Diamond Bar, CA, USA), radiofrequency was performed using a standard irrigated-tip ablation catheter (Thermocool SmartTouch SF, or ThermoCool SmartTouch Navi-star, Biosense Webster), pulmonary vein isolation (PVI), left atrial posterior wall isolation, mitral isthmus linear ablation, and a bidirectional conduction block of the PV, left atrial posterior wall, and mitral isthmus during sinus rhythm.

Follow-up

All patients underwent a systematic follow-up on a set schedule, surface ECG and 24-h Holter monitoring data were recorded after the procedure at an interval of every 3 months or whenever palpitation symptoms appeared, and telephone interviews were conducted quarterly for all patients.

Statistical analysis

Continuous variables were reported as mean \pm standard deviation and compared using an analysis of variance test. Categorical variables are here expressed as frequencies and percentages and compared using Fisher's exact test. All of the data were processed using SPSS (version 21.0 SPSS Inc Chicago, IL, USA). A P -value < 0.05 was considered to be significant.

Results

From January 2020 to January 2022, 176 patients with persistent AF underwent catheter ablation in our center. We included 9 patients in Group A, 38 in Group B, and 12 in Group C. Clinical characteristics are shown in Table 1.

Women were extremely dominant in Groups A and C, the ventricular rate was lower, and CHA₂DS₂-VASC scores were higher in Groups A and C than in Group B. Patients in Groups A and C tended to be older and were more likely to have hypertension, and no difference in clinical characteristics was observed between Groups A and C.

The electrophysiological findings are shown in Table 2. The impedance in Group A was lower than that in Group B. For all the patients in Group A, potentials recorded in the CS multipolar electrode catheter were iso-potentials and lacked high-frequency potentials after deployment of the catheter (Figure 2). Potentials in PVs were deficient or lacked high-frequency potentials (Figure 3). The local potential and impedance decreased rapidly during ablation in Group A (Figure 4). At the end of the procedure, all of the patients experienced restored sinus rhythm; the rate of sinus rhythm was lower in Groups A and C, with four junctional rhythms in Group A. Fifteen cases of atrioventricular (AV) block after restoration of sinus rhythm, and one case of second-degree AV block in Group C. Others were first-degree AV block. AV blocks were more common in Group A, and AF recurrence and maintenance were more common at a very early stage (before discharge) in Group A than in the other groups.

All of the patients were followed up for a mean of 13 months (IQR: 8, 17); the endpoints of follow-up are shown in Table 3; in the latest follow-up, sinus rhythm maintenance was observed in 22% of the patients in Group A, compared with 97% and 83% in Groups B and C, respectively. Only recurrence in Group B was related to the recrudescence of hyperthyroidism in cases in which hyperthyroidism had been under control before ablation; two deaths were recorded, one in Group A and one in Group C, both sudden deaths; two patients in Group A and two more in Group C underwent pacemaker implantation due to sick sinus syndrome; the diameter of the LA decreased in 62% and 67% of patients in Groups B and C, but none of those in Group A.

Discussion

LA fibrosis in PeAF was found to be associated with female sex, high CHADS2VA2S scores, low ventricular rates, age > 70 years, and hypertension also showed a trend of LA fibrosis, which is consistent with the fact that old age and hypertension are both components of the CHADS2VA2S score.

The most interesting finding is that the AF recurrence rate was highest in fibrotic but unenlarged LA, even higher than in cases with both fibrotic and enlarged LA. Beyond PVI and linear ablation in patients without fibrosis. More aggressive ablations, including ablation of fragmental potentials, and isolation of LAA and SVC were performed in patients with fibrosis; however, very early stage recurrence and failure of sinus rhythm maintenance were still much more common in patients with fibrosis, especially those with unenlarged LA.

As sinus rhythm continues, even patients with enlarged and fibrotic LA would experience remodeled LA reversion (8).

In a previous study, fine fibrillatory (f) waves were found to be related to LA fibrosis (9); however, fine (f) waves are difficult to define, and consensus among different electrophysiologists is difficult in daily work.

We would have expected that LA fibrosis would be related to the duration of AF. However, we were not able to collect data or perform any analysis of this because many of the patients in this study had a blurry or inaccurate AF history, which was very common in our area.

Enlarged LA has been treated as a predictor of LA fibrosis and AF recurrence in previous studies (10,11). However, in this study, we noticed that some cases of unenlarged LA showed comprehensive fibrosis and poor prognosis. We developed two hypotheses to explain this: one is that some patients may have enlarged LA during the early stage, which later shrinks toward the end stage of fibrosis; another is that enlarged LA and fibrosis may be secondary to AF, while AF may be secondary to primary LA fibrosis without leaving the diameter unchanged, which explains why patients with fibrotic and enlarged LA paradoxically had better outcomes than those with fibrotic but unenlarged LA.

The ablation of PeAF in elderly women showed the worst outcomes, which indicates that women may require intervention during the early stage of AF (12-15). To prevent failure of ablation and achieve better outcomes, we recommend intensive screening for AF and aggressive intervention for paroxysmal AF in elderly women.

For patients with fibrotic but unenlarged LA, ablation showed little benefit and should be avoided. The issue becomes how to identify such patients before ablation becomes essential. When an electrophysiologist provides an elderly woman with AF the choice of ablation, they should discuss all concerns and evaluations, even if an unenlarged LA is visible.

Limitations

We defined LA fibrosis by electrophysiological findings of low voltage during mapping instead of MRI evaluation of LA before ablation; the sample size was relatively small, as we tended to avoid ablation in the patients that fit the criteria we set.

Conclusions

Comprehensive fibrosis was visible in the unenlarged LA in patients with fibrotic PeAF, but the unenlarged LA was more likely to be seen in women with high CHADS2VA2S scores, indicating poor outcomes for AF ablation.

Declaration

Ethics approval and consent to participate

Our study received the proper ethical oversight by the Ethics Committee of Chongqing General Hospital. All patients were given full explanations of the procedures, and written informed consent was obtained from each patient.

Consent for publication

All authors gave their consent for publication.

Availability of Data and Material

The relevant data in this article will be shared upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

No funding declared.

Authors' contributions

Biao Fu: Conceptualization, Methodology

Xiaoqin Li: Data curation, Formal analysis, Writing- Original draft

Chun Yin: Visualization, Writing- Reviewing and Editing

Yuan Zhang: Validation, Investigation

Hao Zhang: Software, Investigation.

Wenli Wu: Project administration.

Boli Ran: Supervision.

Xiaoli Li: Formal analysis and Visualization.

Yongjing Xiang: Data curation.

Acknowledgments

We thank LetPub (www.letpub.com) for linguistic assistance during the preparation of this manuscript.

References

1. Chang SL, Tsao HM, Lin YJ, Lo LW, Hu YF, Tuan TC, et al. Characteristics and significance of very early recurrence of atrial fibrillation after catheter ablation. *J Cardiovasc Electrophysiol.* 2011 Nov;22(11):1193-1198.
2. den Uijl DW, Delgado V, Bertini M, Tops LF, Trines SA, van de Veire NR, et al. Impact of left atrial fibrosis and left atrial size on the outcome of catheter ablation for atrial fibrillation. *Heart.* 2011 Nov;97(22):1847-1851.
3. Ammar-Busch S, Buiatti A, Tatzber A, Reents T, Bourrier F, Semmler V, et al. Predictors of low voltage areas in persistent atrial fibrillation: is it really a matter of time? *J Interv Card Electrophysiol.* 2020 Apr;57(3):345-352.
4. Seewöster T, Spampinato RA, Sommer P, Lindemann F, Jahnke C, Paetsch I, et al. Left atrial size and total atrial emptying fraction in atrial fibrillation progression. *Heart Rhythm.* 2019 Nov;16(11):1605-1610.
5. Seewöster T, Kosich F, Sommer P, Bertagnolli L, Hindricks G, Kornej J. Prediction of low-voltage areas using modified APPLE score. *Europace.* 2021 Apr 6;23(4):575-580.
6. Soulat-Dufour L, Lang S, Addetia K, Ederhy S, Adavane-Scheuble S, Chauvet-Droit M, et al. Restoring Sinus Rhythm Reverses Cardiac Remodeling and Reduces Valvular Regurgitation in Patients With Atrial Fibrillation. *J Am Coll Cardiol.* 2022 Mar 15;79(10):951-961.
7. Andrés Lahuerta A, Roberto C, Saiz FJ, Cano Ó, Martínez-Mateu L, Alonso P, et al. Atrial low voltage areas: A comparison between atrial fibrillation and sinus rhythm. *Cardiol J.* 2022;29(2):252-262..

8. Qureshi NA, Kim SJ, Cantwell CD, Afonso VX, Bai W, Ali RL, et al. Voltage during atrial fibrillation is superior to voltage during sinus rhythm in localizing areas of delayed enhancement on magnetic resonance imaging: An assessment of the posterior left atrium in patients with persistent atrial fibrillation. *Heart Rhythm*. 2019 Sep;16(9):1357-1367.
9. Kawaji T, Ogawa H, Hamatani Y, Kato M, Yokomatsu T, Miki S, et al. Fine Fibrillatory Wave as a Risk Factor for Heart Failure Events in Patients With Atrial Fibrillation: The Fushimi Atrial Fibrillation (AF) Registry. *J Am Heart Assoc*. 2022 Apr 5;11(7):e024341.
10. Qiu D, Peng L, Ghista DN, Wong KKL. Left Atrial Remodeling Mechanisms Associated with Atrial Fibrillation. *Cardiovasc Eng Technol*. 2021 Jun;12(3):361-372.
11. Efremidis M, Bazoukis G, Vlachos K, Prappa E, Anastasakis A, Megarisiotou A, et al. Atrial substrate characterization in patients with atrial fibrillation and hypertrophic cardiomyopathy: Evidence for an extensive fibrotic disease. *J Electrocardiol*. 2021 Nov-Dec;69:87-92.
12. Zink MD, Chua W, Zeemering S, di Biase L, Antoni BL, David C, et al. Predictors of recurrence of atrial fibrillation within the first 3 months after ablation. *Europace*. 2020 Sep 1;22(9):1337-1344.
13. Deng H, Shantsila A, Guo P, Potpara TS, Zhan X, Fang X, et al. Sex-related risks of recurrence of atrial fibrillation after ablation: Insights from the Guangzhou Atrial Fibrillation Ablation Registry. *Arch Cardiovasc Dis*. 2019 Mar;112(3):171-179.
14. Shah FA, Mahler N, Winkle SM, Fujikawa P, Nader B, Rodriguez J. A Retrospective Cohort Study on Predictors for Rehospitalizations With Recurrence of Atrial Fibrillation Post-Catheter Ablation for Atrial Fibrillation. *Cureus*. 2021 Jul 21;13(7):e16536.
15. Kiedrowicz RM, Wielusinski M, Wojtarowicz A, Kazmierczak J. Predictors of the voltage derived left atrial fibrosis in patients with long-standing persistent atrial fibrillation. *Cardiol J*. 2022;29(4):660-669.

Hosted file

Figure.docx available at <https://authorea.com/users/593819/articles/628645-low-voltage-in-small-left-atrium-in-patients-with-persistent-atrial-fibrillation-left-atrium-diameter-alone-is-not-always-a-predictor-of-prognosis>

Hosted file

Table.docx available at <https://authorea.com/users/593819/articles/628645-low-voltage-in-small-left-atrium-in-patients-with-persistent-atrial-fibrillation-left-atrium-diameter-alone-is-not-always-a-predictor-of-prognosis>