Percutaneous left atrial appendage occlusion in nonvalvular atrial fibrillation patients with coronary heart disease

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Abstract

Purpose To evaluate the 12-month outcomes of the percutaneous left atrial appendage occlusion (LAAO) procedure in nonvalvular atrial fibrillation (NVAF) patients with coronary heart disease (CAD).

Materials and Methods 51 NVAF patients were consecutively accepted LAAO between June 2015 and July 2017. Patients were divided in two groups: 15 with CAD and 36 without CAD. All patients were followed up at 1st, 3rd, 6th, and 12th month after discharge with transesophageal echocardiography (TEE) examination repeated at the same time.

Results Among these 51 patients (average age 64.4±10.0, 33.3% female), the procedural success rate was 98% (50/51). During 12-month follow-up, there were no hemorrhagic stroke or major bleeding. The risk of thromboembolism based on CHA2DS2-VASc score (3.1±1.6 vs. 5.2±1.1, P<0.001) and the risk of hemorrhage based on HAS-BLED score (2.2±1.2 vs. 3.1±1.0, P=0.009) in CAD group were significantly higher. The incidence of end-point events had no statistical difference between CAD and non-CAD. Compared with CAD patients who accepted long-term antithrombotic medication, there was no obvious difference in stroke rate and mortality in CAD accepted LAAO group, whereas a further reduction of hemorrhage (n=5/20% vs. n=0, P=0.039) was shown. A significant correlation (P<0.001, r=0.580) was detected between moderate or severe left atrial spontaneous echo contrast (LASEC) and the composite end point events.

Conclusion There are similar safety and effectiveness for LAAO procedure in NVAF patients with CAD and without CAD under new oral anticoagulants applied post-implantation anticoagulation strategy. Meanwhile, LASEC is a predictive factor of LAAO in NVAF patients combined CAD.

Background

Atrial fibrillation (AF) is the most common arrhythmia which increased the risk of embolic stroke approximately 5 times [1]. There are over 8 million NVAF patients in China currently, accounting for 0.77% of the Chinese population [2]. LAAO is an alternative approach to stroke prophylaxis especially in patients with contraindication to chronic OAC therapy.

It is reported that approximate 30%-40% of AF patients have concurrent coronary heart disease (CAD). Concomitant CAD may increase the substantial risk of ischemic or hemorrhagic events as well
as the mortality rate associated with AF. Although there has been some subgroup data coming from the previous studies, the LAAO procedure in CAD patients has not been specially investigated to date. Another hot issue about contemporary percutaneous modalities of LAAO is the antithrombotic strategies following device implantation. Even the Watchman is approved 3 months of NOACs therapy instead of warfarin in conjunction with aspirin now [3], the comparison of performance of LAAO with these drugs is still urgently needed.

This retrospective study aimed to describe long term efficacy and safety of the percutaneous LAAO in NVAF patients with CAD in the context of NOACs applied post-implantation strategy, and to compare the performance of LAAO with NOACs in Chinese CAD patients.

**Methods**

**Patients**

Our retrospective single-center study enrolled in 51 patients with NVAF, who underwent LAAO with the Watchman device or LAmbre device between June 2015 and July 2017. The main procedural inclusion were as follows: (1) patients with nonvalvular paroxysmal, persistent, or permanent AF; (2) left ventricular ejection fraction≥30%; (3) CHADS\textsubscript{2} score≥1; (4) cerebral vascular accident history including stroke and transient ischemic attack(TIA) or thromboembolism, even under OAC treatment; (5) without absolute contraindication to warfarin or NOACs. Patients with LAA thrombus, aortic atheroma, carotid disease, intolerant to short-term (at least 3 months) OAC as well as required chronic clopidogrel therapy were excluded. The eligibility criteria were similar to PROTECT AF and PREVAIL trial [4, 5].

**Implantation technique and patient management**

LAAO was performed in coronary angiography lab under general anesthesia in our center. A detailed description of the procedure was published previously [1]. TEE was performed before and throughout the procedure to determine eligibility for LAAO, allow selection of the optimal size of the device, and monitor the complications. NOAC (rivaroxaban or dabigatran) was applied as post-implantation anticoagulation strategy for 3 months in conjunction with aspirin monotherapy. All patients were followed up at 1\textsuperscript{st}, 3\textsuperscript{rd}, 6\textsuperscript{th}, and 12\textsuperscript{th} month after discharge, while TEE examination was repeated. A
follow-up questionnaire based on the Munich Consensus Document was used at each visit time or telephone contract, including mortality (cardiovascular and non-cardiovascular), thromboembolic events (stroke, TIA and systemic embolism) and bleeding (life threatening or disabling, major and minor bleeding).

Data collections
The data retrospectively collected included patient demographics, medical histories and TEE indexes. An adequate LAA sealing defined as residual leak<5mm around the margins of the device, compression ratio of device (Watchman) >9% by TEE. Leaks were categorized into 4 categories: none, complete or < 1mm leak; mild, < 2mm leak; moderate, < 3mm leak; severe, 3-5mm leak.

Thromboembolic risk was estimated by the CHADS<sub>2</sub> score (1 point for: Age≥75 years, Congestive heart failure, Hypertension, Diabetes Mellitus; 2 points for: TIA) and the CHA<sub>2</sub>DS<sub>2</sub>-VAS<sub>C</sub> score (1 point for: Congestive heart failure, Hypertension, Diabetes, Vascular disease, Age 65-74, Female; 2 points for: Age≥75, prior Stroke) , and the bleeding risk was predicted by the HAS-BLED score (1 point for: Hypertension, Abnormal renal/liver function, Stroke, Bleeding, Labile INRs, Elderly, Drugs and alcohol).

For the objective of study, patients were divided into two groups: CAD group and non-CAD group. We defined a combination of death, DVT, stroke, bleeding as a composite end-point.

Statistical analysis
Continuous variables were expressed as mean ± SD, and comparisons between groups were made using the Student t test. Categorical variables were described as count and percentage, and comparisons between groups were made using the chi-square test or the Fisher exact test, whenever necessary. Spearman bivariate correlate analysis was used to explore the correlation between LASEC (which was based on grade in previous study [6]) and composite end point. Statistics were analyzed using SPSS (version 23.0, IBM Software, USA). A p value<0.05 (two-tailed) was considered as statistically significant.

Results
Demographic characteristics
LAAO procedure were performed in 51 patients (34 male and 17 female) with mean age of 64.4±10.0.
Of all the patients, the 29.4% (15/51) of patients have concomitant CAD. The anticoagulation policies before LAAO were highly heterogeneous, including Vitamin K antagonist, aspirin, clopidogrel, rivaroxaban or dabigatran. Compared to NVAF patients without CAD, patients with CAD were older (62.4±10.6yrs vs. 69.1±6.5yrs, p=0.026) and more likely to have other chronic disease, such as diabetes mellitus (DM) (11.1% vs. 53.3%, p=0.001), chronic heart failure (CHF) (13.9% vs. 40.0%, p=0.041) or chronic obstructive pulmonary disease (COPD) (2.8% vs. 26.7%, p=0.01). The risk of thromboembolism based on CHA\textsubscript{2}DS\textsubscript{2} score (2.5±1.4 vs. 2.0±1.3, p<0.001) or CHA\textsubscript{2}DS\textsubscript{2}-VASc score (3.1±1.6 vs. 5.2±1.1, p<0.001) and the risk of hemorrhage based on HAS-BLED score (2.2±1.2 vs. 3.1±1.0, p=0.009) were significantly higher in CAD group (Table 1).

Procedure results

The devices were implanted successfully in 50 patients, with a procedural success rate of 98% (50/51). There was no procedure related stroke, bleeding or cardiac tamponade. One patient did not wake up from general anesthesia, and died 7 days after procedure due to procedure related thromboembolism. The incidence of pericardial effusion was 15.7% (8/51).

The mean diameter of the LAA ostium was 23.3±3.7mm, and the most popular morphology of LAA was cactus with 2-3 lobes. Watchman was the first selected device, with which majority (47/92.2%) of patients were implanted. Two common sizes of watchman were 27mm (20/39.2%) and 30mm (13/25.5%). The rate of device compression was 20.4±4.6. The 32 (62.7%) patients presented trivial residual leak (≤1mm), and no large residual leak (>5mm) was observed. The LAmbre device was implanted in 4 patients (7.8%) as an alternative for the shallow or broad profile of LAA which was not suitable for occlusion with Watchman. Among 51 NVAF patients, 4 patients received combined procedures with Watchman device implantation after AF ablation, and 4 patients underwent combined procedures with transcatheter closure of ASD with Amplatzer device post LAAO with Wachaman device successfully. After LAAO all patients were prescribed rivaroxaban (22/44%) or dabigatran (28/56%) for 3 months as temporary anticoagulation protocols, followed by aspirin monotherapy.

Transesophageal echocardiography characteristics

There were no significant differences in lobes, morphology, and dimension of LAA between CAD group
and non-CAD group, while EF values were obviously lower in patients with CAD. Meanwhile, there were no significant differences in device type, residual leak immediately after procedure, and post LAAO anticoagulation medications between two groups (Table 2).

**Follow-up results**

During 12-month follow-up period, there were no hemorrhagic stroke or major bleeding. Two patients developed device related thrombus (DRT) that resolved by additional anticoagulation without any ischemic events. Two patients experienced transient ischemic stroke. There were three patients died overall: one for procedure related thromboembolism, one for pneumonia, and one for pancreatic cancer. There were no statistical difference in incidence of stroke, bleeding, DRT and cardiovascular death between the CAD group and non-CAD group during the whole follow-up. Nevertheless the all-cause death (n=0 vs. n=3/21.4%, \( p=0.006 \)) in CAD group was particularly higher, which could be ascribed to the more critical state of illness (Table 3).

Compared with NVAF combined CAD patients who accepted long-term NOACs treatment as thromboembolism prophylaxis, there were no obviously differences in stroke rate and mortality in NVAF combined CAD patients accepted LAAO group, whereas a further reduction of hemorrhage (n=5/20% vs. n=0, \( p=0.039 \)) was shown (Table 4).

In patients with end-point events, CHA\(_2\)DS\(_2\)-VASc score, HAS-BLED score and mean LVEF had no difference from patients without end-point events (CHA\(_2\)DS\(_2\)-VASc \( p=0.051 \); HAS-BLED \( p=0.995 \); LVEF \( p=0.853 \)). The LAA pulsed wave peak velocity, which reflected the LAA function, obviously decreased in patients with end-point events (45.00±13.06 vs. 62.61±11.89 cm/s \( p=0.001 \)). Worth to say, the percentage of moderate or severe LASEC in end-point events group was significantly higher than without end-point events group (46.6% vs. 13.8%, \( p=0.01 \), Fig1 and Fig2). In SEC positive group, the patients’ LAA pulsed wave peak velocity was importantly decreased than SEC negative group (45.83±9.42 vs. 64.62±11.20 cm/s, \( p<0.001 \)), meaning the functional degeneration of LAA. A significantly correlation (\( p<0.001 \), \( r=0.580 \)) was detected between moderate or severe LASEC and the composite end points (death, stroke, bleeding and DRT).

**Discussion**
This analysis represented 51 cases of the percutaneous LAAO in Chinese NVAF patients in real world, and 1-year follow-up data from these patients. To our knowledge, this study is the first to assess LAAO procedure in NVAF patients combined with coronary heart disease.

The main findings of this investigation are: first, the reduction of thromboembolic risk after LAAO was similar in patients with CAD compared to patients without CAD but LAAO benefit more in CAD patients who had higher risk of hemorrhage; second, the anticoagulation protocol of 3-month NOACs followed by aspirin monotherapy after LAAO didn’t increase the risk of stroke rate and mortality but reduced the risk of hemorrhage in 12-month follow-up; third, LASEC had a significant correlation with the composite end points, declaring that it could be a predictive factor of LAAO in NVAF patients with CAD.

The left atrial appendage (LAA) is a muscular, tubular structure of the primordial left atrium. Although most its features and variations are still unclear, studies confirmed that 90% of thrombus originated from LAA [7]. LAA occlusion in patients with AF at the time of cardiac surgery was initially reported to be related with lower risk of readmission for thromboembolism and all-cause mortality over subsequent 3 years, providing an inspiration of percutaneous LAAO [8]. The LAAO procedure has become a proper strategy for stroke prophylaxis regardless of patients’ age so far. Some data from China also proved the efficiency and safety for NVAF to prevent the incidence of stroke in Chinese patients [9]. There are demonstrations about different percutaneous LAAO devices, including: (1) Watchman (Boston Scientific); (2) LAmbre (Lifetech); (3) Coherex WaveCrest (Johnson & Johnson); (4) LARIAT device (SentreHEART); (5) Amplatzer cardiac plug and Amulet (Abbott Vascular); (6) Ultraceal (Cardia) [10]. A meta-analysis has already proved the efficacy and safety of LAAO as an alternative approach for NVAF patients that seek non-pharmacologic therapy for stroke prevention, with a high implantation success rate of 96.3% and a pooled proportion of procedure-related mortality rate of 0.28% [11]. The LAAO patients we incorporated had different operation devices (Watchman and LAmbre) as well as a rich variety of operation methods, such as single percutaneous LAAO, AF ablation plus LAAO and ASD closure plus LAAO. The efficacy and safety of percutaneous LAAO in our team was well established by the 98% success and almost 0% mortality in these different kinds of
NVAF patients, which was similar to previous studies.

As most common combination disease of AF, our study reported that the NVAF patients with CAD had higher risk of thromboembolism and hemorrhage than those without CAD. Indeed, the Framingham study had shown that prevalent cardiovascular disease was an independent risk factor for AF [12]. It is well known that in patients receiving coronary bypass, post-operative AF is a highly independent risk factor for thrombotic stroke, with rates from 2% to 7%. A specific antithrombotic strategy after LAAO in CAD patients is urgently warranted. Through previous innovation and iteration, dual antiplatelet therapy (DAPT), as well as NOACs plus aspirin for at least 3 months were approved as antithrombotic strategies following Watchman implantation, with ischemic stroke rate of 1.4% and major bleeding rate of 2.5% at 1 year [13]. In a single center real-world experience of the prospective Global Amulet Registry, average DRT rate was 0.9%, with the lowest rates in DAPT group (0.5%) and the highest in NOAC group (2.0%), indicating the efficacy and safety of this antithrombotic option following Amulet implantation [14]. It was surprised that 21 patients showed no DRT despite not having received any antithrombotic therapy [14]. After one year follow up, more than 80% patients discharged with single aspirin therapy, but did not appear to have a higher risk of device-related thrombus [15]. In the vast majority of cases for other devices, DAPT lasted from 1 to 6 months [3]. The EP Wire survey revealed that in patients with and without device thrombosis, early- and long-term anticoagulation options following device implantation were very heterogeneous among centres, due to most strategies not being supported by the randomized trials [16]. According these previous clinical researches, we approved 3 months of NOACs therapy in conjunction with aspirin alternatively. There were no statistical difference in incidence of stroke, bleeding, DRT and cardiovascular death between the CAD group and non-CAD group during the whole follow-up.

It's worth mentioning in our investigation, the percentage of moderate or severe LASEC in end-point events group was significantly higher than without end-point events group, and a significantly correlation was detected between moderate or severe LASEC and the composite end points, meaning LASEC was a predictive factor of LAAO in NVAF patients with CAD. In previous studies, presence of LASEC, decreased LAA emptying velocity, or thrombus, has been reported as markers of
thromboembolic risk in NVAF [17]. SEC was defined as smoke-like substance with a characteristic swirling motion persisting throughout the whole cardiac cycle [18]. As we know, the ejection fraction and the CHA2DS2-VASc score were proved as independent predictive factors of both left atrial thrombi and SEC [19]. Evenmore, as an independent risk predictor, the number of LAA lobes has a moderate predictive value for LASEC in patients with NVAF [17]. It was reported that stroke incidence significantly increased with the severity of LASEC (7.9% for grade 1, 14.3% for grade 2, and 30.8% for grade 3, respectively) [20]. This was confirmed by our study. The anticoagulant strategy should be individualized and consolidated in SEC positive patients with NVAF combined CAD. One study from Japan showed that Compared to dabigatran (110 mg twice daily) group, the warfarin group owned more grade 2 or more severe patients with LASEC, indicating that dabigatran may be more effective for reducing LASEC as compared with warfarin [6]. In our study, all the patients received NOACs followed aspirin as a post-operation anticoagulant strategy, this strategy may be extended or adjusted in LASEC positive patients until ensuring proper device endothelialization.

There are several limitations associated with this study. First, this study is a single-center study, enrolling a relatively minority of patients. Second, the retrospective design of the study is an additional limitation, leading to information bias in analysis. Third, treatment dose of NOACs was not carefully evaluated and we didn’t analysis the events in different LASEC groups. A large-scale, randomized, prospective study is necessary to prove the results listed in this study.

Conclusions
LAAO procedures for NVAF patients with CAD has similar safety endpoints and long-term efficacy as patients without CAD in the circumstance of NOACs applied post-implantation anticoagulation strategy. Meanwhile, LASEC is a predictive factor of LAAO in NVAF patients with CAD. Special attention should be paid to high-risk CAD NVAF patients to reduce the all-cause mortality.

Abbreviations
Declarations

Ethics approval and consent to participate

All procedures performed in this study involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study informed consent is not required. This study was approved by the ethics committee of Nanjing First Hospital.

Consent for publication

Consent for publication was obtained for every individual person’s data included in the study.

Availability of data and materials

The data and materials supporting the results and conclusion of this study was available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

ZL designed the statistical analysis and revised the manuscript. XDJ and ZL were responsible for LAAO procedure in every patients. LJ participated in the data collection and follow-up survey. ZJ and JXM were responsible for TEE in patients and were the main contributors in writing the manuscript. All authors read and approved the final manuscript.

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References

1. Bartus K, Han FT, Bednarek J, Myc J, Kapelak B, Sadowski J et al. Percutaneous left atrial appendage suture ligation using the LARIAT device in patients with atrial fibrillation: initial clinical experience. Journal of the American College of Cardiology. 2013;62(2):108-18. doi:10.1016/j.jacc.2012.06.046.

2. Wilke T, Groth A, Mueller S, Pfannkuche M, Verheyen F, Linder R et al. Incidence and prevalence of atrial fibrillation: an analysis based on 8.3 million patients. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2013;15(4):486-93. doi:10.1093/europace/eus333.

3. Chen S, Weise FK, Chun KRJ, Schmidt B. Antithrombotic strategies after interventional left atrial appendage closure: an update. Expert review of cardiovascular therapy. 2018;16(9):675-8. doi:10.1080/14779072.2018.1510316.

4. Holmes DR, Jr., Kar S, Price MJ, Whisenant B, Sievert H, Doshi SK et al. Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. Journal of the American College of Cardiology. 2014;64(1):1-12. doi:10.1016/j.jacc.2014.04.029.

5. Holmes DR, Reddy VY, Turi ZG, Doshi SK, Sievert H, Buchbinder M et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet (London, England). 2009;374(9689):534-42. doi:10.1016/s0140-6736(09)61343-x.

6. Watanabe T, Shinoda Y, Ikeoka K, Inui H, Fukuoka H, Sunaga A et al. Dabigatran exhibits low intensity of left atrial spontaneous echo contrast in patients with
nonvalvular atrial fibrillation as compared with warfarin. Heart and vessels. 2017;32(3):326-32. doi:10.1007/s00380-016-0871-5.

7. Beigel R, Wunderlich NC, Ho SY, Arsanjani R, Siegel RJ. The left atrial appendage: anatomy, function, and noninvasive evaluation. JACC Cardiovascular imaging. 2014;7(12):1251-65. doi:10.1016/j.jcmg.2014.08.009.

8. Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. The Annals of thoracic surgery. 1996;61(2):755-9. doi:10.1016/0003-4975(95)00887-x.

9. Huang WP, Zhang YH, He L, Su X, Yang XW, Guo ZX. Efficacy and Safety of the WATCHMAN Left Atrial Appendage System for Stroke Prevention in Chinese Patients with Nonvalvular Atrial Fibrillation: A Single-center, Prospective, Observational Study. Chinese medical journal. 2017;130(4):434-8. doi:10.4103/0366-6999.199832.

10. Cruz-Gonzalez I, Fuertes-Barahona M, Moreno-Samos JC, Gonzalez-Ferreiro R, Lam YY, Sanchez PL. Left Atrial Appendage Occlusion: The Current Device Landscape and Future Perspectives. Interventional cardiology clinics. 2018;7(2):253-65. doi:10.1016/j.iccl.2017.12.011.

11. Yerasi C, Lazkani M, Kolluru P, Miryala V, Kim J, Moole H et al. An updated systematic review and meta-analysis of early outcomes after left atrial appendage occlusion. Journal of interventional cardiology. 2018;31(2):197-206. doi:10.1111/jioc.12502.

12. Schnabel RB, Sullivan LM, Levy D, Pencina MJ, Massaro JM, D'Agostino RB, Sr. et al. Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study. Lancet (London, England). 2009;373(9665):739-45. doi:10.1016/s0140-6736(09)60443-8.

13. Bergmann MW, Ince H, Kische S, Schmitz T, Meincke F, Schmidt B et al. Real-world safety and efficacy of WATCHMAN LAA closure at one year in patients on dual
antiplatelet therapy: results of the DAPT subgroup from the EWOLUTION all-comers study. EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2018;13(17):2003-11. doi:10.4244/eij-d-17-00672.

14. Landmesser U, Schmidt B, Nielsen-Kudsk JE, Lam SCC, Park JW, Tarantini G et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: periprocedural and early clinical/echocardiographic data from a global prospective observational study. EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2017;13(7):867-76. doi:10.4244/eij-d-17-00493.

15. Landmesser U, Tondo C, Camm J, Diener HC, Paul V, Schmidt B et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: one-year follow-up from the prospective global Amulet observational registry. EuroIntervention : journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2018;14(5):e590-e7. doi:10.4244/eij-d-18-00344.

16. Tilz RR, Potpara T, Chen J, Dobreanu D, Larsen TB, Haugaa KH et al. Left atrial appendage occluder implantation in Europe: indications and anticoagulation post-implantation. Results of the European Heart Rhythm Association Survey. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2017;19(10):1737-42. doi:10.1093/europace/eux254.

17. Wang F, Zhu M, Wang X, Zhang W, Su Y, Lu Y et al. Predictive value of left atrial appendage lobes on left atrial thrombus or spontaneous echo contrast in patients with non-valvular atrial fibrillation. BMC cardiovascular disorders. 2018;18(1):153. doi:10.1186/s12872-018-0889-y.
18. Watson T, Shantsila E, Lip GY. Mechanisms of thrombogenesis in atrial fibrillation: Virchow's triad revisited. Lancet (London, England). 2009;373(9658):155-66. doi:10.1016/s0140-6736(09)60040-4.

19. Bejinariu AG, Hartel DU, Brockmeier J, Oeckinghaus R, Herzer A, Tebbe U. Left atrial thrombi and spontaneous echo contrast in patients with atrial fibrillation: Systematic analysis of a single-center experience. Herz. 2016;41(8):706-14. doi:10.1007/s00059-016-4423-7.

20. Zhao Y, Ji L, Liu J, Wu J, Wang Y, Shen S et al. Intensity of Left Atrial Spontaneous Echo Contrast as a Correlate for Stroke Risk Stratification in Patients with Nonvalvular Atrial Fibrillation. Scientific reports. 2016;6:27650. doi:10.1038/srep27650.

Tables

(Table1) **Baseline characteristics and risk factors of patients**

|                        | Total (n=51) | Non-CAD (n=36) | CAD (n=15) | p value |
|------------------------|-------------|----------------|-----------|--------|
| **Female, n (%)**      | 17 (33.3%)  | 14 (38.1%)     | 3 (20.0%) | 0.197  |
| **Age, yrs**           | 64.4±10.0   | 62.4±10.6      | 69.1±6.5  | 0.026  |
| **Age≥75yrs n (%)**    | 5 (9.8%)    | 3 (8.3%)       | 2 (13.3%) | 0.588  |
| **AF**                 |             |                |           |        |
| Paroxysmal AF, n (%)   | 16 (31.4%)  | 12 (33.3%)     | 4 (26.7%) | 0.643  |
| Permanent/Persistent   | 35 (68.6%)  | 24 (66.7%)     | 11 (73.3%)|        |
| **DM, n (%)**          | 12 (23.5%)  | 4 (11.1%)      | 8 (53.3%) | 0.001  |
| **ASD, n (%)**         | 4 (7.8%)    | 4 (11.1%)      | 0         | 0.183  |
| **CHF, n (%)**         | 11 (21.6%)  | 5 (13.9%)      | 6 (40.0%) | 0.041  |
| **EH, n (%)**          | 29 (56.9%)  | 18 (50.0%)     | 11 (73.3%)| 0.129  |
| **Previous stroke/TIA, n (%)** | 30 (58.8%) | 19 (52.8%)     | 11 (73.3%)| 0.178  |
| **Previous PCI, n (%)** | 8 (15.7%)   | 0              | 8 (53.3%) | <0.001 |
| **HOCOM, n (%)**       | 3 (5.9%)    | 3 (8.3%)       | 0         | 0.254  |
| **COPD, n (%)**        | 5 (9.8%)    | 1 (2.8%)       | 4 (26.7%) | 0.010  |
| **Scr, umol/L**        | 76.2±16.5   | 73.2±14.9      | 83.3±18.7 | 0.044  |
| **Medications before LAOO** |         |                |           |        |
| Vitamin K antagonist, n (%) | 16 (31.4%) | 10 (27.8%)     | 6 (40.0%) | 0.260  |
| Aspirin, n (%)         | 4 (7.8%)    | 4 (11.1%)      | 0         |        |
| Clopidogrel, n (%)     | 2 (3.9%)    | 1 (2.8%)       | 1 (6.7%)  |        |
| Aspirin + clopidogrel, n (%) | 5 (9.8%) | 1 (2.8%)       | 4 (26.7%) |        |
| Vitamin K antagonist + Aspirin, n (%) | 1 (2.0%) | 0 | 1 (6.7%) |        |
| **Rivaroxaban, n (%)** | 11 (21.6%)  | 11 (30.6%)     | 0         |        |
| Dabigatran, n (%)      | 12 (23.5%)  | 9 (25.0%)      | 3 (20.0%) |        |
| CHADS2                 | 2.5±1.4     | 2.0±1.3       | 3.5±0.8   | <0.001 |
| **CHA2DS2-VASc**       | 3.7±1.7     | 3.1±1.6       | 5.1±0.9   | <0.001 |
| HAS-BLED               | 2.4±1.2     | 2.1±1.2       | 3.1±1.0   | 0.005  |
## Table2: Comparison of baseline TEE characteristics and Procedure/in-hospital adverse events between with/without CAD groups

|                        | Total (n=51) | Non-CAD (n=36) | CAD (n=15) | p value |
|------------------------|--------------|----------------|------------|---------|
| **Morphology of LAA**  |              |                |            |         |
| Cauliflower, n (%)     | 13 (22.5%)   | 10 (27.8%)     | 3 (20.0%)  | 0.136   |
| Chicken-wings, n (%)   | 15 (29.4%)   | 12 (33.3%)     | 3 (20.0%)  |         |
| Cactus, n (%)          | 21 (41.2%)   | 14 (38.9%)     | 7 (46.7%)  |         |
| Wind-sleeve, n (%)     | 2 (3.9%)     | 0              | 2 (13.3%)  |         |
| **Lobes**              |              |                |            |         |
| 1, n (%)               | 8 (15.7%)    | 5 (13.9%)      | 3 (20.0%)  | 0.268   |
| 2, n (%)               | 21 (41.2%)   | 13 (36.1%)     | 8 (53.3%)  |         |
| 3, n (%)               | 17 (33.3%)   | 15 (41.7%)     | 2 (13.3%)  |         |
| 4, n (%)               | 5 (9.8%)     | 3 (8.3%)       | 2 (13.3%)  |         |
| **Maximum LAA ostium width, mm** |         | 23.3±3.6        | 23.3±3.6   | 0.943   |
| **Maximum LAA length, mm** |         | 27.2±4.8       | 26.6±4.9   | 0.159   |
| **LAA emptying velocity, cm/s** |         | 56.3±14.9      | 60.9±14.2  | 0.159   |
| **Mean LA diameter, mm** |         | 49.1±4.2       | 48.6±4.2   | 0.176   |
| **LVEF, %**            | 59.9±9.0     | 61.9±6.8       | 55.0±11.8  | 0.048   |
| **One-stop operation, n (%)** |         | 12 (23.5%)     | 5 (13.8%)  | 0.01    |
| **Device type**        |              |                |            |         |
| LAMbre, n (%)          | 4 (7.8%)     | 3 (8.3%)       | 1 (6.7%)   | 0.842   |
| WatchMAN, n (%)        | 47 (92.2%)   | 33 (91.7%)     | 14 (93.3%) |         |
| 24mm, n (%)            | 9 (17.6%)    | 6 (16.2%)      | 3 (20.0%)  | 0.580   |
| 27mm, n (%)            | 13 (25.5%)   | 11 (30.6%)     | 2 (13.3%)  |         |
| 30mm, n (%)            | 5 (9.8%)     | 3 (8.3%)       | 2 (13.3%)  |         |
| 33mm, n (%)            |              |                |            |         |
| **Leak**               |              |                |            |         |
| Complete or <1mm, n (%)| 32 (62.7%)   | 22 (61.1%)     | 10 (66.7%) | 0.648   |
| <2mm, n (%)            | 11 (21.6%)   | 8 (22.2%)      | 3 (20.0%)  |         |
| <3mm, n (%)            | 5 (9.8%)     | 3 (8.3%)       | 2 (13.3%)  |         |
| 3-5mm, n (%)           | 3 (5.9%)     | 3 (8.3%)       | 0          |         |
| **Pericardial effusion, n (%)** |         | 8 (15.7%)      | 4 (11.1%)  | 0.124   |
| **Compression ratio of occlude, %** |         | 20.4±4.6       | 21.0±4.9   | 0.209   |
| **Maximum off-the-shoulder, mm** |         | 2.6±2.4        | 2.5±2.3    | 0.620   |
| **Procedure related stroke/TIA, n (%)** |         | 0              | 0          | NS      |
| **Procedure related bleeding, n (%)** |         | 0              | 0          | NS      |
| **Procedure related death, n (%)** |         | 1 (2.0%)       | 1 (6.7%)   | 0.121   |
| **Procedure related tromboembolism** |         | 1 (2.0%)       | 0          | 1 (6.7%) |
| **Anticoagulation post LAO, n** |         | 50             | 36         | 14      |
| Rivaroxaban, n (%)     | 22 (44%)     | 18 (50.0%)     | 4 (28.5%)  | 0.175   |
| Dabigatran, n (%)      | 28 (56%)     | 18 (50.0%)     | 10 (71.4%) |         |

## Table3: Comparison of TEE characteristics and adverse events between with/without CAD groups during 1 year follow-up
|                              | Total  (n=51) | Non-CAD (n=36) | CAD (n=15) | p value |
|------------------------------|--------------|----------------|------------|---------|
| Mean LA diameter, mm         | 50.9±4.5     | 50.5±4.5       | 52.0±4.6   | 0.347   |
| Compression ratio of occlude, % | 18.7±4.2   | 19.2±4.7       | 17.2±1.5   | 0.179   |
| Leak Complete or <1mm, n (%) | 27 (62.8%)   | 19 (59.4%)     | 8 (72.7%)  | 0.468   |
| <2mm, n (%)                  | 8 (18.6%)    | 7 (21.9%)      | 1 (9.1%)   |         |
| <3mm, n (%)                  | 5 (11.6%)    | 3 (9.4%)       | 2 (18.2%)  |         |
| 3-5mm, n (%)                 | 3 (7.0%)     | 3 (9.4%)       | 0          |         |
| Maximum off-the-shoulder, mm | 2.2±2.1      | 2.2±2.1        | 2.3±2.2    | 0.912   |
| Pericardial effusion, n (%)  | 2 (4.7%)     | 2 (6.3%)       | 0          | 0.401   |
| Medications at 1 year        |              |                |            |         |
| None, n (%)                  | 2 (4.2%)     | 2 (5.6%)       | 0          | 0.679   |
| Vitamin K antagonist, n (%)  | 2 (4.2%)     | 1 (2.8%)       | 1 (8.3%)   |         |
| Aspirin, n (%)               | 42 (87.5%)   | 31 (86.1%)     | 11 (91.7%) |         |
| Rivaroxaban, n (%)           | 1 (2.1%)     | 1 (2.8%)       |            |         |
| Dabigatran, n (%)            | 1 (2.1%)     | 1 (2.8%)       |            |         |
| ALL stroke n (%)             | 2 (4.3%)     | 1 (2.8%)       | 1 (9.1%)   | 0.369   |
| Ischemic Stroke/TIA, n (%)   | 2 (4.3%)     | 1 (2.8%)       | 1 (9.1%)   |         |
| Hemorrhagic stroke, n (%)    | 0            | 0              |            |         |
| Disabling stroke, n (%)      | 0            | 0              |            |         |
| Nondisabling stroke, n (%)   | 2 (4.3%)     | 1 (2.8%)       | 1 (9.1%)   |         |
| Bleeding, all n (%)          | 1(2.0%)      | 1(2.8%)        | 0          | 0.510   |
| Life threatening/disable bleeding, n (%) | 0 | 0 | 0 |         |
| Major bleeding, n (%)        | 0            | 0              | 0          |         |
| Minor bleeding, n (%)        | 1 (2.0%)     | 1 (2.8%)       | 0          |         |
| All-cause death, all n (%)   | 3 (6.0%)     | 0              | 3 (21.4%)  | 0.006   |
| Cardiovascular death, n (%)  | 0            | 0              | 1 (7.1%)   | 0.121   |
| Non-cardiovascular, n (%)    | 2 (4.0%)     | 0              | 2 (14.3%)  |         |
| Device related thrombus, n (%) | 2 (3.9%)    | 2 (5.6%)       | 0          | 0.356   |
(Table 4) Comparison of Baseline characteristics and adverse events during 1 year follow-up between LAAO and Control group in CAD patients

|                                | control (n=20) | LAAO (n=15) | p value |
|--------------------------------|----------------|-------------|---------|
| **Baseline**                   |                |             |         |
| Female, n (%)                  | 10 (50.0%)     | 3 (20.0%)   | 0.073   |
| Age, yrs                       | 67.1±10.1      | 69.1±6.5    | 0.489   |
| PCI, n (%)                     | 5(25.0%)       | 8(53.3%)    | 0.091   |
| AF                             |                |             |         |
| Paroxysmal AF, n (%)           | 7 (35.0%)      | 4 (26.7%)   | 0.604   |
| Permanent /Persistent AF, n (%)| 13 (65.0%)     | 11 (73.3%)  |         |
| **Anticoagulation at baseline/post LAAO** | | | |
| Aspirin + Rivaroxaban, n (%)   | 2(10.0%)       | 0           | 0.438   |
| Rivaroxaban, n (%)             | 8 (40.0%)      | 4(26.7%)    |         |
| Dabigatran, n (%)              | 10 (50.0%)     | 10 (66.7%)  |         |
| CHADS2                         | 2.9±1.2        | 3.5±0.8     | 0.111   |
| CHA2DS2-VASc                   | 4.4±1.9        | 5.1±0.9     | 0.144   |
| HAS-BLED                       | 2.8±1.2        | 3.1±1.0     | 0.310   |
| **1-year follow up, n (%)**    |                |             |         |
| ALL stroke n (%)               | 2 (10.0%)      | 1 (9.1%)    | 0.878   |
| Ischemic Stroke/TIA, n (%)     | 2 (10.0%)      | 1 (9.1%)    |         |
| Hemorrhagic stroke, n (%)      | 0              | 0           |         |
| Disabling stroke, n (%)        | 0              | 0           |         |
| Nondisabling stroke, n (%)     | 2 (10.0%)      | 1 (9.1%)    |         |
| **Bleeding, all n (%)**        |                |             |         |
| Life threatening/major bleeding, n (%) | 5 (20.0%) | 0 | 0.039 |
| Minor bleeding, n (%)          | 3 (10.0%)      | 0           |         |
| **All-cause death, all n (%)** |                |             |         |
| Cardiovascular death, n (%)    | 1 (5.0%)       | 1 (7.1%)    |         |
| Non-cardiovascular, n (%)      | 1 (5.0%)       | 2 (14.3%)   |         |

Figures
Figure 1

LASEC grade distribution of patients with and without composite end-point events (*
P<0.01).
Two patients with DRT (A, B) were respectively found to have corresponding grade 2 (C) and grade 3 (D) SEC in preoperative TEE examination.

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.
Table5sup.docx