Feasibility and Safety of Extended Posterior Wall Isolation Technique of Laser Balloon Ablation for Paroxysmal Atrial Fibrillation

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Abstract

Background Laser balloon ablation (LBA) is a balloon-based catheter ablation technology used for atrial fibrillation (AF) ablation in recent years. The laser balloon has the potential to extend the isolation area because of its changeable balloon size. The purpose of the study was to investigate the feasibility and safety of extended LBA technique, and to compare the isolation area with an established balloon technique using the cryoballoon ablation (CBA). Methods From June 2020 to July 2021, 76 consecutive patients with paroxysmal AF who underwent initial pulmonary vein isolation were enrolled. Of these, 65 patients were included in the study, excluding 11 who met the exclusion criteria; 32 and 33 patients were in the LBA and CBA groups, respectively. In the LBA group, after standard ablation of each PV, additional extended posterior wall ablation was performed by increasing the balloon size to the maximum (the extended LBA technique). In the CBA group, cryoablation was performed using a 28-mm balloon. In both groups, voltage maps were created for measuring the isolated surface area (ISA) by the CARTO mapping system pre- and post-ablation. Results In the LBA group, the extended LBA technique was feasible in all patients. The total ISA after the extended LBA technique was significantly larger than before $(32.4\pm6.5 \text{ vs } 22.3\pm4.1 \text{ cm}^2,$ p < 0.001) and the non-isolated posterior wall area was significantly smaller ($8.9 \pm 3.5 \text{ vs} 13.3 \pm 3.7 \text{ cm}^2$, p < 0.001). Although the percentage of esophageal temperature elevation (>39.0°C) was higher during the extended LBA than during the standard LBA (LIPV: 26/32 [81%] vs. 7/32 [22%], p<0.001; LSPV: 10/32 [31%] vs. 2/32 [6%], p<0.001), symptomatic gastric hypomotility or esophageal mucosal injury was not observed in all patients. Comparing the extended LBA and the CBA group, IASA-R (18.1 \pm 4.6 vs 15.9 \pm 3.5, p=0.033) and non-isolated posterior wall (8.9 \pm 3.5 vs 12.4 \pm 3.7, p<0.001) were significantly greater in the extended LBA, but cardiac enzyme elevation after ablation was lower than the CBA group. No significant differences were found between the two groups in perioperative major complications or AF-free survival at 3 and 6 months. Conclusions LBA with extended posterior wall isolation technique was safe and feasible. Long-term effectiveness studies should be evaluated in a larger sample size.

Original article

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Abstract

Background

Laser balloon ablation (LBA) is a balloon-based catheter ablation technology used for atrial fibrillation (AF) ablation in recent years. The laser balloon has the potential to extend the isolation area because of its changeable balloon size. The purpose of the study was to investigate the feasibility and safety of extended LBA technique, and to compare the isolation area with an established balloon technique using the cryoballoon ablation (CBA).

Methods

From June 2020 to July 2021, 76 consecutive patients with paroxysmal AF who underwent initial pulmonary vein isolation were enrolled. Of these, 65 patients were included in the study, excluding 11 who met the exclusion criteria; 32 and 33 patients were in the LBA and CBA groups, respectively. In the LBA group, after standard ablation of each PV, additional extended posterior wall ablation was performed by increasing the balloon size to the maximum (the extended LBA technique). In the CBA group, cryoablation was performed using a 28-mm balloon. In both groups, voltage maps were created for measuring the isolated surface area (ISA) by the CARTO mapping system pre- and post-ablation.

Results

In the LBA group, the extended LBA technique was feasible in all patients. The total ISA after the extended LBA technique was significantly larger than before $(32.4\pm6.5 \text{ vs } 22.3\pm4.1 \text{ cm}^2, \text{p}<0.001)$ and the non-isolated posterior wall area was significantly smaller $(8.9 \pm 3.5 \text{ vs } 13.3 \pm 3.7 \text{ cm}2, \text{p}<0.001)$. Although the percentage of esophageal temperature elevation $(>39.0^{\circ}\text{C})$ was higher during the extended LBA than during the standard LBA (LIPV: 26/32 [81%] vs. 7/32 [22%], p<0.001; LSPV: 10/32 [31%] vs. 2/32 [6%], p<0.001), symptomatic gastric hypomotility or esophageal mucosal injury was not observed in all patients. Comparing the extended LBA and the CBA group, IASA-R ($18.1 \pm 4.6 \text{ vs } 15.9 \pm 3.5, \text{p}=0.033$) and non-isolated posterior wall (8.9 $\pm 3.5 \text{ vs } 12.4 \pm 3.7, \text{p}<0.001$) were significantly greater in the extended LBA, but cardiac enzyme elevation after ablation was lower than the CBA group. No significant differences were found between the two groups in perioperative major complications or AF-free survival at 3 and 6 months.

Conclusions

LBA with extended posterior wall isolation technique was safe and feasible. Long-term effectiveness studies should be evaluated in a larger sample size.

Keywords : atrial fibrillation, catheter ablation, Laser balloon, Cryoballoon, posterior wall.

Introduction

Pulmonary vein isolation (PVI) is an effective treatment for atrial fibrillation (AF). Recent advances in balloon-based ablation systems utilizing various energy sources have offered several alternative approaches to facilitate AF ablation procedure. Visually guided laser balloon (VGLB) uniquely incorporates laser as the ablative energy source and a 2F fiber-optic endoscope that allows lesion delivery under direct visualization of the PV lumen. Previous studies demonstrated that the VGLB and radiofrequency ablation systems are equally effective for paroxysmal AF. Pulmonary vein (PV) is the major site of ectopic foci initiating paroxysmal atrial fibrillation (PAF), and isolation of PV from atrial tissue can cure 60% to 70% of patients with PAF. Several studies also addressed the importance of non-PV ectopic beats initiating PAF, and non-PV ectopic beats originated from left atrial posterior free wall (LAPW) are relatively common; for example, LAPW (38.0%), superior vena cava (37.0%), ligament of Marshall (8.2%) and crista terminalis (3.7%).

Although extensive PVI is reported to be significantly superior to segmental PVI in terms of AF recurrence rate because ectopy can be removed from LAPW, extensive PVI is difficult to achieve with balloon-based ablation systems. However, the laser balloon has the potential to extend the isolation area because of its changeable balloon size. The objectives of this study were to determine 1) whether it is safe and feasible to extend the laser balloon to its maximum diameter after standard LBA for additional ablation of the posterior wall, 2) whether the isolation area of posterior wall after extended posterior wall isolation is greater than before, and 3) whether the posterior wall is largely isolated by comparing the isolation area of posterior wall with other balloon-based ablation systems, cryoballoon ablation (CBA).

Methods

Study Patients

From June 2020 to July 2021, consecutive patients with paroxysmal AF who underwent initial pulmonary vein isolation were enrolled; enrollment in the LBA group was done at Koseikai Takeda Hospital, and enrollment in the CBA group at Kyoto Prefectural University of Medicine, respectively. This study included paroxysmal AF patients aged 20 years or older. Written informed consent was provided to all patients prior to study enrollment. The study was approved by the Institutional Review Board of University of Hospital Kyoto Prefectural University of Medicine. Exclusion criteria for this study were as follows; Patients who had undergone previous PVI, patients with a left atrial diameter of 55 mm or greater, patients with a common PV trunk, and patients who required touch-up ablation.

Ablation Procedure

Before the procedure, a contrast-enhanced computerized tomography (CT) scan was conducted to visualize the anatomy of the left atrium and PVs. In all patients, an esophageal temperature probe was inserted to monitor luminal esophageal temperature. If luminal esophageal temperature reached the predefined safety cutoff temperature (cryoballoon: 20 and laser balloon: 39), ablation was prematurely terminated. A 6Fr 20-pole three site mapping catheter (BeeAT, Japan-Lifeline Co, Ltd, Tokyo, Japan) was positioned in a coronary sinus via the right subclavian vein or the right femoral vein for pacing, recording, and internal cardioversion. After vascular access was obtained, a single transseptal puncture was performed using a radiofrequency needle (Baylis Medical, Inc, Montreal, QC, Canada) and 8-Fr long sheath (SL0, AF Division, St Jude Medical). Heparinized saline was additionally infused to maintain the activated clotting time at 300-350s. The right PN was continuously paced from the superior cava vein during right phrenic nerve (PN) in order to avoid right phrenic nerve injury (PNI). In the case of loss of PN capture or cessation or weakening of right hemidiaphragm contractions, energy delivery was immediately terminated.

Laser balloon Ablation

LBA was performed under deep sedation using boluses of fentanyl and a continuous infusion of propofol and dexmedetomidine. The transseptal sheath was exchanged over a guidewire for 12-Fr steerable sheath (Cardio Focus). The LB (first generation) was navigated to each individual PV using the steerable sheath and inflated to obtain optimal PV occlusion (pulmonary vein occlusion Grade 1). In this study, the balloon size (the balloon size is dynamic as a function of pressure used to provide inflation) was increased from Step 1 to 9, and the laser balloon was slowly inflated from Step 1 until optimal pulmonary vein occlusion was obtained. Laser energy was deployed in a point-by-point fashion thereby covering 30deg of a circle with each ablation lesion. According to the degree of tissue exposure 12 to 5.5 W overlapping beams along with corresponding 20 to 30 seconds duration was attempted (Standard LBA; Figure 1A). Furthermore, the balloon size was increased to the maximum size (the balloon size was Step 9, which is the maximum size recommended by the Cardio Focus), and the anterior and posterior walls were enlarged so that the balloon-tissue contact was maximized regardless of the size of the target PV ostium (Extended LBA; Figure 1B).

Cryoballoon Ablation

CBA was performed under deep sedation using a continuous infusion of propofol. The transseptal sheath was exchanged over a guidewire for 15-Fr steerable sheath (Flexcath Advance, Medtronic, Minneapolis, MN). The transseptal sheath was exchanged over a guidewire for a 15-Fr steerable sheath (Flexcath Advance, Medtronic). The third generation cryoballoon was inserted into the left atrium guided by a spiral catheter (SC, Achieve, 20mm, Medtronic, Minneapolis, MN). Following the confirmation of complete sealing of the PV with a 28-mm CB using a contrast medium injection, a freeze cycle of 180seconds was applied. If the esophageal temperature fell below 20, or if there was a decrease or loss of diaphragmatic pacing capture, the freezing time was less than 180 seconds. A bonus freeze of 150-180 seconds duration was applied if the freezing time was short or if the pulmonary vein potential remained.

High density LA voltage mapping

The three-dimensional geometry of LA and PVs was reconstructed using the CARTO (Biosense Webster, Irvine, CA, USA) navigation system. High density bipolar voltage mapping was performed using a 20pole steerable mapping catheter (Pentaray, Biosense Webster) during atrial pacing at coronary sinus. LA voltage mapping (more than 1500 mapping points were obtained per time) was performed three times before treatment, after standard LBA, and after extended LBA in the LBA group, and twice before and after CBA in the CBA group.

Measurement and Definition of the isolation area

The PV ostium was defined as the point of maximal inflection between the PV wall and the left atrial wall. The isolation areas were defined as low voltage areas (<0.5 mV) evaluated by high resolution mapping. The PV antrum area was defined as the antral surface area excluding the PVs. The corresponding PV antrum

area was defined as the isolated antral surface areas (IASA). The total IASA (IASA-T, cm²) was defined as the sum of the left-sided IASA (IASA-L, cm²) and right-sided IASA (IASA-R, cm²). The non-isolated LA posterior wall surface area (LAPW, cm²) was defined as the area delineated by the upper and lower line, connecting the most superior and inferior aspect of the non-isolated area. (Figure 2). The relative size of the isolation area, the isolated surface area (ISA) was computed using the following formula: ISA (%) =IASA-T/(IASA-T+LAPW) x100. Using the manually selected points, the surface areas were calculated automatically by the CARTO3 system. To assess inter- and intra-observer variability, left-sided and right-sided IASA and non-isolated posterior wall area were independently assessed by three electrophysiologists. The electrophysiologists were blinded to each of the technology used.

Follow-up

During hospitalization, the measurement of Troponin I, CK, CK-MB, WBC and CRP were collected before the ablation and one day after the ablation. All patients underwent routine follow-up at our outpatient clinic, where clinical evaluation was performed. A 24-hour Holter recording was obtained at 3 and 6 months after ablation, respectively; the blanking period was 3 months. Recurrence was defined as any symptomatic or documented atrial arrhythmia lasting > 30 seconds. Antiarrhythmic drugs were prescribed at the discretion of physicians during the follow-up.

Statistical Analysis

Continuous date is expressed as the mean +- standard deviation for normally distributed variables or as the median (25th, 75th percentiles) for non-normally distributed variables. Differences in continuous variables between the LBA group and the CBA group were analyzed by Student t test or Mann-Whitney U test. Difference in dichotomous variables were analyzed by χ^2 test. The isolation areas by 2 different ablation techniques in the same patient were compared using a paired t test or Wilcoxon signed-rank test. The P value presented is for a 2-tailed test. A P value of <0.05 indicated statistical significance. Analyses were conducted using JMP 14 software (SAS Institute, Cary, NC).

Results

Patient characteristics

A total of 76 patients were enrolled between June 2020 and July 2021, and 35 and 41 patients underwent LBA and CBA, respectively. In the LBA group, 3 patients were excluded due to missing blood sampling data. In the CBA group, 3 patients were excluded due to the need for touch-up, 1 patient due to withdrawal of consent, 3 patients due to missing blood sampling data, and 1 patient due to insufficient mapping data. Finally, a total of 65 patients (32 in the LBA group and 33 in the CBA group) were analyzed. Patient characteristics and echocardiographic measurements are shown in **Table 1**. Age (LBA; 67.9 \pm 8.2 vs CBA; 66.5 \pm 10.7, p=0.57), female (LBA; 28% vs CBA; 21%, p=0.52), normal EF (defined as LVEF>55%) (LBA; 90% vs CBA; 91%, p=0.97), left atrial diameter (LBA; 38.9 \pm 6.8 vs CBA; 36.7 \pm 4.3, p=0.12) were not significantly different between two groups.

Procedural data

The number of laser balloon applications per vein was twice in all patients among the LBA group. The balloon size during the standard LBA was 4-5 for the left superior pulmonary vein (LSPV), 5-7 for the right superior pulmonary vein (RSPV), 2-5 for the left inferior pulmonary vein (LIPV), 2-5 for the right inferior pulmonary vein (RIPV), with optimal pulmonary vein occlusion. During the extended LBA, the balloon size could be increased to the maximum size (Step 9) for most of the PVs. For only one PV in a patient, balloon size was downsized to Step 7 because Step 9 did not provide good balloon-tissue contact. All 32 patients successfully underwent the extended LBA after the standard LBA. After the extended LBA, IASA-L (14.3±2.8 vs 10.5±3.0 cm², p<0.001) and IASA-R (18.1±4.6 vs 11.8±2.8 cm², p<0.001), and the IASA-T (32.4±6.5 versus 22.3±4.1 cm², p<0.001) were all significantly larger compared with the standard LBA. Non-isolated posterior wall area was significantly smaller in the extended LBA than before (8.9±3.5 vs 13.3±3.7 cm², p<0.001), and ISA was significantly greater than before (78.2±8.4% vs 62.8±8.9%, p<0.001).

Although a higher percentage of esophageal temperatures rose above 39.0° C in the extended LBA compared to the standard LBA (LIPV: 26/32 [81%] vs 7/32 [22%], p<0.0001, and LSPV: 10/32 [31%] vs 2/32 [6%], p<0.0001), no symptomatic gastric hypomotility or esophageal mucosal injury was observed.

In the CBA group, the mean number of cryoballoon freezes were 1.4 ± 0.6 , 1.4 ± 0.5 , 1.2 ± 0.4 , 1.2 ± 0.4 applications for LSPV, LIPV, RSPV, RIPV, respectively, with complete PVI.

Compared to the CBA, the IASA-L, IASA-R and IASA-T during the extended LBA were as follows: the extended LBA vs the CBA; 14.3 ± 2.8 vs 14.3 ± 3.0 , p=0.97, 18.1 ± 4.5 vs 15.9 ± 3.5 , p=0.033, and 32.4 ± 6.5 vs 30.2 ± 4.7 cm², p=0.12, respectively. Non-isolated posterior wall area was significantly smaller in the extended LBA than in the CBA (8.9 ± 3.5 vs 12.4 ± 3.7 cm², p<0.001), and ISA was significantly greater than in the CBA ($78.2\pm8.4\%$ vs $71.0\pm6.2\%$, p<0.001). (**Table 2**)

Right phrenic nerve injury occurred in 2 patients in the LBA and 1 in the CBA. The phrenic nerve injury fully recovered 6 months after the procedure. There was 1 stroke in the LBA, but no death or cardiac tamponade was observed in either group. Procedure time and LA dwelling time were significantly longer in the LBA compared with the CBA (178 ± 39 vs 113 ± 27 min, P<0.001 and 144 ± 37 vs 81 ± 21 min, p<0.001). Fluoroscopy time was significantly shorter in the LBA compared with the CBA (26 ± 9 vs 36 ± 13 , p=0.001).

Follow-up

The time course of inflammation and myocardial damage markers before and after ablation is shown in **Table 3**. The baseline data for each parameter were not significantly different between the two groups. The rate of increase in Troponin I, CK and CK-MB on the day after ablation were significantly lower in the LBA than in the CBA, but no significant difference in inflammatory markers were observed between the two groups.

Adherence to the follow-up protocol was 97%, 63 of 65 patients (LBA; n=32, CBA; n=31) completed scheduled visits, including Holter monitoring. The freedom from any atrial arrhythmia was 97% (31/32) and 91% (29/32) in the LBA vs 87% (27/31) and 84% (26/31) in the CBA at 3 and 6 months, respectively (p=0.45).

Discussion

The main findings of this study are as follows. The extended posterior wall ablation technique, which increases the posterior wall ablation area by increasing the balloon size of the LB after the standard LBA, is the first attempt to our knowledge. The addition of the extended LBA technique significantly increased the isolated area compared to the standard LBA in all patients, but the increase in cardiac enzyme after the extended LBA was significantly less than that of the CBA. Although esophageal temperature elevation was frequently observed during the extended LBA, no clinically significant esophageal injury was observed.

Feasibility of the extended posterior wall ablation technique

Several studies have compared isolated areas of ablation using balloon technology. In those studies, CBA was reported to have a greater isolation area than LBA. The laser balloon is a compliant and soft balloon that can easily penetrate deep into the pulmonary veins, resulting in a smaller isolation area. It is also thought that the smaller balloon is easier to obtain adequate pulmonary vein occlusion and that the choice of the smaller balloon size by the operator may have influenced the results. In agreement with previous studies, the present study showed that the standard LBA had smaller isolation areas than CBA.

After the extended LBA technique, the increase in isolation area of the right PV was significantly larger than that of the left PV. The main reason is that when the laser balloon is pushed in an expanded position during RPV ablation, the axis of the balloon is parallel to the posterior wall side and tends to adhere to the posterior wall. A larger isolated posterior wall area has been reported to have a lower recurrence rate after AF ablation. Since this study is a feasibility study of our method, long-term results are out of scope, but we hope that this method will contribute to reducing the recurrence rate of AF in the future.

Safety of the extended posterior wall ablation technique

LBA has been reported to be equivalent in safety to radiofrequency ablation and CBA. In the present study, no serious perioperative complications such as cardiac tamponade, left atrial-esophageal fistula, or death occurred. Although the risk of diaphragmatic palsy is high in all balloon procedures, the incidence of transient diaphragmatic palsy was low in the present study: 6% in the LBA and 3% in the CBA. One case of cerebral infarction occurred in the LBA, but the patient was discharged home with only mild paralysis. No patient in the LBA complained of gastrointestinal symptoms and only one patient in the CBA complained of gastrointestinal symptoms and stomach after ablation , and in our study, all patients were prescribed PPI or H2 blockers, and esophageal temperature was carefully monitored during ablation, which prevented symptomatic esophageal injury.

The potential of the extended posterior wall ablation technique

It is known that an increased inflammatory response after ablation is associated with an early recurrence of atrial fibrillation. Recently, Yano et al, showed that inflammatory markers (CRP, WBC) on the day after ablation were higher in the LBA than in the CBA, and therefore the early recurrence rate was higher in the LBA. In our study, although there was an increase in inflammatory response markers (CRP, WBC) on the day after ablation in both the LBA and CBA, no significant difference was seen between the two groups. Studies on the inflammatory response to laser balloon ablation are few (ref 22 and our study only) and controversial, but may depend on difference in speed of increase in inflammatory response between the LBA and the CBA, the number of ablation procedures, and the timing of blood sampling measurements. On the other hand, biomarkers of myocardial injury (troponin I, CK, and CK-MB) were significantly lower in the LBA; the balloon contact area to the tissues in the CBA was wider than the linear lesions formed by photonic energy delivery in the LBA, so biomarkers of myocardial injury are considered significantly higher in the CBA.

Limitation

This feasibility study has limitations that should be acknowledged. First, esophageal endoscopy was not performed in study patients, so subclinical esophageal injury related to observed esophageal heating cannot be excluded. In addition, our study is too small to estimate the probability of atrioesophageal fistula after the extended LBA. Second, as this work focused on procedural success rates and safety, there few data available on long-term efficacy and freedom of AF. Moreover, the sample size of our study was quite small and the study was not powered to investigate difference in clinical outcome. Our findings should be verified in a randomized prospective study.

Conclusion

LBA with extended posterior wall isolation technique was safe and feasible. The mid-term efficacy with extended LBA is high with an AF-free rate of 91%. This strategy requires further study in a larger number of patients to observe long-term AF-free rate.

References

1. Kuck KH, Brugada J, Fürnkranz A, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. N Engl J Med. 2016;374:2235-2245. doi:10.1056/NEJMoa1602014 2. Yamaguchi Y, Sohara H, Takeda H, et al. Long-Term Results of Radiofrequency Hot Balloon Ablation in Patients with Paroxysmal Atrial Fibrillation: Safety and Rhythm Outcomes. Journal of Cardiovascular Electrophysiology. 2015;26(12):1298-1306. doi:10.1111/jce.12820 3. Schmidt B, Gunawardene M, Urban V, et al. Visually guided sequential pulmonary vein isolation: Insights into techniques and predictors of acute success. Journal of Cardiovascular Electrophysiology. 2012;23(6):576-582. doi:10.1111/j.1540-8167.2011.02247.x 4. Dukkipati SR, Kuck KH, Neuzil P, et al. Pulmonary vein isolation using a visually guided laser balloon catheter the first 200-patient multicenter clinical experience. Circulation: Arrhythmia and Electrophysiology. 2013;6(3):467-472. doi:10.1161/CIRCEP.113.000431 5. Reynolds MR, Zheng Q, Doros G. Laser balloon ablation for AF: A systematic review and meta-analysis. Journal of Cardiovascular Electrophysiology. 2018:29(10):1363-1370. doi:10.1111/jce.13698 6. Haïssaguerre M, Jaïs P, Shah D C, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med. 1998;339(10):659-666. 7. Chen SA, Hsieh MH, Tai CT, et al. Initiation of Atrial Fibrillation by Ectopic Beats Originating From the Pulmonary Veins Electrophysiological Characteristics, Pharmacological Responses, and Effects of Radiofrequency Ablation. Circulation. 1999;100(18):1879-1886. http://www.circulationaha.org 8. Chen SA, Tai CT, Wen-Chung YU, et al. Right Atrial Focal Atrial Fibrillation: Electrophysiologic Characteristics and Radiofrequency Catheter Ablation. J Cardiovasc Electrophysiol. 1999;10(3):328-335. 9. Tsai CF, Tai CT, Hsieh MH, et al. Initiation of Atrial Fibrillation by Ectopic Beats Originating From the Superior Vena Cava Electrophysiological Characteristics and Results of Radiofrequency Ablation. Circulation. 2000;102(1):67-74. http://www.circulationaha.org 10. Hwang C, Wu TJ, Doshi RN, Peter CT, Chen PS. Vein of Marshall Cannulation for the Analysis of Electrical Activity in Patients With Focal Atrial Fibrillation. Circulation. 2000;101(13):1503-1508. http://www.circulationaha.org 11. Lin WS, Tai CT, Hsieh MH, et al. Catheter ablation of paroxysmal atrial fibrillation initiated by non-pulmonary vein ectopy. Circulation. 2003;107(25):3176-3183. doi:10.1161/01.CIR.0000074206.52056.2D 12. Nagase T, Bordignon S, Perrotta L, et al. Analysis of procedural data of pulmonary vein isolation for atrial fibrillation with the second-generation laser balloon. PACE - Pacing and Clinical Electrophysiology. 2019;42(7):837-845. doi:10.1111/pace.13692 13. Perrotta L, Konstantinou A, Bordignon S, et al. What is the acute antral lesion size after pulmonary vein isolation using different balloon ablation technologies? Circulation Journal. 2017;81(2):172-179. doi:10.1253/circj.CJ-16-0345 14. Nagashima K, Okumura Y, Watanabe I, et al. Hot Balloon Versus Cryoballoon Ablation for Atrial Fibrillation: Lesion Characteristics and Middle-Term Outcomes. Circulation Arrhythmia and electrophysiology. 2018;11(5):e005861. doi:10.1161/CIRCEP.117.005861 15. Kiuchi K, Kircher S, Watanabe N, et al. Quantitative analysis of isolation area and rhythm outcome in patients with paroxysmal atrial fibrillation after circumferential pulmonary vein antrum isolation using the pace-and-ablate technique. Circulation: Arrhythmia and Electrophysiology. 2012;5(4):667-675. doi:10.1161/CIRCEP.111.969923 16. Yoshimura S, Kaseno K. Kimura K, et al. Impact of the size of non-ablated left atrial posterior wall area on outcomes after extensive encircling pulmonary vein isolation. Heart and Vessels. 2021;36(9):1421-1429. doi:10.1007/s00380-021-01820-3 17. Chun JKR, Bordignon S, Last J, et al. Cryoballoon Versus Laserballoon: Insights from the First Prospective Randomized Balloon Trial in Catheter Ablation of Atrial Fibrillation. Circulation: Arrhythmia and Electrophysiology. 2021; (February):119-127. doi:10.1161/CIRCEP.120.009294 18. Tachibana S, Okishige K, Sudo K, et al. Predictors of phrenic nerve injury during pulmonary vein isolation for curing atrial fibrillation with balloon-based visually guided laser ablation. Circulation Journal. 2021;85(3):275-282. doi:10.1253/circj.CJ-20-0953 19. Cordes F, Ellermann C, Dechering DG, et al. Pre-procedural proton pump inhibition is associated with fewer peri-oesophageal lesions after cryoballoon pulmonary vein isolation. Scientific Reports. 2021;11(1). doi:10.1038/s41598-021-83928-0 20. Kovama T, Sekiguchi Y, Tada H, et al. Comparison of Characteristics and Significance of Immediate Versus Early Versus No Recurrence of Atrial Fibrillation After Catheter Ablation. American Journal of Cardiology. 2009;103(9):1249-1254. doi:10.1016/j.amjcard.2009.01.010 21. Richter B, Gwechenberger M, Socas A, et al. Markers of oxidative stress after ablation of atrial fibrillation are associated with inflammation, delivered radiofrequency energy and early recurrence of atrial fibrillation. Clinical Research in Cardiology. 2012;101(3):217-225. doi:10.1007/s00392-011-0383-3 22. Yano M, Egami Y, Ukita K, et al. Impact of myocardial injury and inflammation due to ablation on the short-term and mid-term outcomes: Cryoballoon versus laser balloon ablation. International Journal of Cardiology. 2021;338:102-108. doi:10.1016/j.ijcard.2021.06.016 23. Casella M, Russo A dello, Russo E, et al. Biomarkers of myocardial injury with different energy sources for atrial fibrillation catheter ablation. Cardiology Journal. 2014;21(5):516-523. doi:10.5603/CJ.a2013.0153

Tables

Table 1. Clinical characteristics of the study pati

		LBA Group	CBA Group	
	Total (n=65)	(n=32)	(n=33)	P value
Clinical				
characteristics				
Age, y	67.9 ± 9.5	67.9 ± 8.2	66.5 ± 10.7	0.57
Female	16(25%)	9(28%)	7 (21%)	0.52
$BMI, kg/m^2$	23.9 ± 2.9	23.9 ± 3.1	24.0 ± 2.8	0.90
Heart failure	6(9%)	1(3%)	5(15%)	0.094
Hypertension	31 (48%)	19 (59%)	12 (36%)	0.63
Diabetes mellitus	11 (17%)	7(22%)	4 (12%)	0.29
Prior stroke/TIA	1 (2%)	1 (3%)	0 (0%)	0.31
Echocardiographic				
measurements				
LVEF > 55%	59(91%)	29 (90%)	30 (91%)	0.97
Left atrial	37.8 ± 7.7	38.9 ± 6.8	36.7 ± 4.3	0.12
diameter, mm				

BMI, body mass index; CBA, cryoballoon ablation; LBA, Laser balloon ablation; LVEF, left ventricular ejection fraction; TIA, transient ischemic attack.

Table 2. Comparison of the isolated surface area between 3 Ablation techniques

	Group 1 Extended LBA (n=32)	Group 2 Standard LBA (n=32)	Group 3 CBA (n=
IASA-L, cm2	14.3 ± 2.8	10.5 ± 2.4	14.3 ± 3.0
IASA-R, cm2	18.1 ± 4.6	11.8 ± 2.8	15.9 ± 3.5
IASA-T, cm2	32.4 ± 6.5	22.3 ± 4.1	30.2 ± 4.7
Non-isolated PW, cm2	8.9 ± 3.5	13.3 ± 3.7	12.4 ± 3.7
ISA, $\%$	78.2 ± 8.4	62.8 ± 8.9	71.0 ± 6.2

ISA, isolated surface area; IASA-L, left-sided isolated antral surface area; IASA-R, right-sided isolated antral surface area; IASA-T, total isolated antral surface area; PW, posterior wall; ISA = IASA-T/ (IASA-T+Non-isolated PW) $\times 100$)

Table 3. Time course of acute inflammation markers in the Laser balloon and Cryoballoon ablation.

		LBA Group $(n-32)$	LBA Group $(n-32)$	CBA Group $(n-32)$	D voluo
		(11-52)	(11-52)	(11-55)	1 value
Before	Before				
Ablation	Ablation				
Troponin I,	Troponin I,	0.04 ± 0.02	0.04 ± 0.02	0.04 ± 0.00	0.21
$\mu g/l$	$\mu \mathrm{g/l}$				
CK, IU/l	CK, IU/l	108 ± 71	108 ± 71	122 ± 52	0.35
CK-MB, IU/l	9.9 ± 3.5	9.9 ± 3.5	3.7 ± 2.3	< 0.001	
CRP, mg/dl	CRP, mg/dl	0.22 ± 0.09	0.22 ± 0.09	0.09 ± 0.13	0.20
WBC, $/\mu l$	WBC, $/\mu l$	5612 ± 1359	5612 ± 1359	5300 ± 1217	0.33
The day	The day				
after	after				
Ablation	Ablation				

		LBA Group (n=32)	LBA Group (n=32)	CBA Group (n=33)	P value
Troponin Ι, μg/l	Troponin I, µg/l	7.73 ± 3.34	7.73 ± 3.34	9.98 ± 5.00	0.037
CK, IU/l	CK, IU/l	176 ± 95	176 ± 95	350 ± 126	< 0.001
CK-MB, IU/l	CK-MB, IU/l	18.0 ± 5.5	18.0 ± 5.5	30.1 ± 12.0	< 0.001
CRP, mg/dl WBC, $/\mu$ l	CRP, mg/dl WBC, $/\mu l$	$\begin{array}{c} 0.82 \pm 0.89 \\ 9181 \pm 2391 \end{array}$	$\begin{array}{c} 0.82 \pm 0.89 \\ 9181 \pm 2391 \end{array}$	$\begin{array}{c} 0.86 \pm 0.62 \\ 8267 \pm 1824 \end{array}$	$0.82 \\ 0.087$

CBA, Cryoballoon ablation; CK, Creatine Kinase; CRP, C-reactive protein; LBA, Laser balloon ablation; WBC, white blood cell.

Figures

Figure 1A : Standard Laser balloon ablation.

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Legend: The Laser balloon is placed at the LSPV, RSPV, LIPV, RIPV ostium with optimal occlusion. The balloon size is 4-7 for the LSPV, 5-7 for the RSPV, 2-6 for the LIPV, 3-5 for the RIPV.

LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.

Figure 1B: Extended Laser balloon ablation.

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Legend: The Laser balloon is placed at the LSPV, RSPV, LIPV, RIPV ostium with the maximum balloon size. The balloon size is 9 for the LSPV, 9 for the RSPV, 9 for the LIPV, 7-9 for the RIPV.

LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.

Figure 2. Post-ablation voltage measurement and identification.

Legend: On the voltage map, the purple areas are high-voltage zones with a bipolar electrogram amplitude ≥ 0.5 mV. The red, orange, yellow, green, and blue area is low-voltage zones with a bipolar electrogram amplitude ≤ 0.5 mV, that is isolated area.

IASA-L, left isolated antral surface area; IASA-R, right isolated antral surface area; LIPV, left inferior pulmonary vein; LSPV, left superior pulmonary vein; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein.