# Hot balloon vs. cryoballoon ablation for persistent atrial fibrillation: lesion area, efficacy, and safety

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April 28, 2020



**Abstract**

Introduction: The clinical efficacy and safety of hot balloon ablation (HBA) for treatment of persistent AF (PerAF) remain unclear. We aimed to evaluate the clinical efficacy and safety of HBA vs. cryoballoon ablation (CBA) as treatment for PerAF. Methods: Of 195 consecutive patients who underwent initial catheter ablation for PerAF (AF lasting >7 days but <12 months), 158 propensity score-matched (79 HBA and 79 CBA) patients were included in our study. All patients who underwent HBA received applications of energy to the upper posterior LA wall with a larger balloon in addition to single shots to each pulmonary vein (PV) ostium, whereas those who underwent CBA received simple single-shot applications. The electrically isolated surface area (ISA), including the PV antrum and part of the posterior LA wall, was assessed by high-resolution mapping. Results: Success of the PV isolation with balloon shots alone did not differ between HBA and CBA (81% vs. 85%; P = 0.52). The ISA was generally wide in both groups and significantly larger in the HBA group than in the CBA group (61 ± 16% vs. 51 ± 12%, P < 0.001). The incidence of procedure-related complications did not differ significantly (HBA 4% vs. CBA 1%; P = 0.62) nor did the arrhythmia recurrence rate (HBA 11% vs. CBA 18% at 18 months; P = 0.26). Conclusion: Despite the difference in protocols, HBA and CBA performed for PerAF appear comparable in terms of wide antral lesion creation, clinical efficacy, and safety.

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The study was supported by departmental resources only, and the authors have no conflict of interest to declare.

Short title: Hotballoon vs. Cryoballoon Ablation for persistent AF

# ABSTRACT

**Introduction:** The clinical efficacy and safety of hot balloon ablation (HBA) for treatment of persistent AF (PerAF) remain unclear. We aimed to evaluate the clinical efficacy and safety of HBA vs. cryoballoon ablation (CBA) as treatment for PerAF.

**Methods:** Of 195 consecutive patients who underwent initial catheter ablation for PerAF (AF lasting >7 days but <12 months), 158 propensity score-matched (79 HBA and 79 CBA) patients were included in our study. All patients who underwent HBA received applications of energy to the upper posterior LA wall with a larger balloon in addition to single shots to each pulmonary vein (PV) ostium, whereas those who underwent CBA received simple single-shot applications. The electrically isolated surface area (ISA), including the PV antrum and part of the posterior LA wall, was assessed by high-resolution mapping.

**Results:** Success of the PV isolation with balloon shots alone did not differ between HBA and CBA (81% vs. 85%; $P = 0.52$). The ISA was generally wide in both groups and significantly larger in the HBA group than in the CBA group (61 ± 16% vs. 51 ± 12%, $P< 0.001$). The incidence of procedure-related complications did not differ significantly (HBA 4% vs. CBA 1%; $P = 0.62$) nor did the arrhythmia recurrence rate (HBA 11% vs. CBA 18% at 18 months;$P = 0.26$).

**Conclusion** : Despite the difference in protocols, HBA and CBA performed for PerAF appear comparable in terms of wide antral lesion creation, clinical efficacy, and safety.

**KEYWORDS**

Cryoballoon; Hotballoon, Persistent atrial fibrillation

**ABBREVIATIONS**

AF=atrial fibrillation

CBA=cryoballoon ablation

HBA=hotballoon ablation

LA=left atrium or left atrial

PerAF=persistent AF

# INTRODUCTION

Balloon-based pulmonary vein isolation (PVI), whether hot balloon ablation (HBA) or cryoballoon ablation (CBA), is a widely accepted therapeutic strategy for atrial fibrillation (AF). Reported clinical outcomes of HBA and CBA for paroxysmal AF are equally good despite the fact that CBA produces wider ablation areas than those produced by HBA.[1] Several recently reported studies have shown the clinical utility of CBA for persistent AF (PerAF); outcomes are similar to those obtained by conventional radiofrequency (RF) ablation.[2,3]However, the clinical efficacy and safety of HBA in cases of PerAF remain undetermined.

Therefore, we conducted a retrospective study in which we compared the ablation area, complications, and clinical outcomes of HBA and CBA performed for PerAF.

# METHODS

## Study patients

One hundred fifty-eight patients were included in the study. These patients were drawn from a pool of 195 consecutive patients (152 men, 42 women; aged 64 ± 10 years) who had undergone balloon-based ablation (HBA, n=103; CBA, n=92) for PerAF at Dokkyo Medical University Saitama Medical Center or Nihon University Itabashi Hospital between June 2015 and January 2019. PerAF was defined as AF lasting [?]7 days but <12 months, and no patient with long-standing PerAF (AF lasting >12 months) was included. So that a study comparing HBA and CBA could be performed. the total patients were assigned propensity scores, which accounted for age, sex, body mass index, $CHA_2DS_2$-VASc score, left atrial diameter (LAD), and left ventricular ejection fraction (LVEF). Nearest neighbor matching within a 0.2 caliper width and 1:1 matching ratio issued in 2 study groups of 79 patients each. The institutional review boards at Dokkyo Medical University Saitama Medical Center Bioethics Committee and Nihon University Hospital Ethics Committee approved the collection and review of these data.

## Preparation for Ablation

For all patients, antiarrhythmic drugs (AADs) were discontinued for at least 5 half-lives prior to the ablation procedure. Conscious sedation was achieved with dexmedetomidine, propofol, and fentanyl. Vascular access was obtained, a single transseptal puncture guided by intra-cardiac ultrasound, was performed, and intravenous heparin was administered to maintain an activated clotting time of >300 seconds. Three-dimensional maps of the LA and 4 PVs were created with the NavX system (Abbott Laboratories, Abbott Park, IL).

## HBA

HBA was performed with the SATAKE HotBalloon ablation system (Toray Industries, Inc., Tokyo, Japan) during AF rhythm, as previously described.[1,4]For PV occlusion, the balloon was inflated to 26–33 mm in diameter with 10–20 mL of contrast medium diluted 1:2 with saline. Once optimal PV occlusion, assessed by contrast angiography, was achieved, a 1.8-MHz RF current was applied between the coil electrode inside the balloon and 4 cutaneous electrode patches on the patient's back to produce capacitive-type balloon heating. The target internal balloon temperature (70oC or 73oC for the left superior PV [LSPV] and 70oC for the other PVs) was maintained by delivery of vibratory waves through the catheter shaft lumen into the balloon to agitate the fluid inside. Because of the relatively high incidence of PV stenosis previously reported,[4] we performed the procedure via antral approach to avoid intra-PV ablation and thus prevent chronic-phase complications. The balloon was positioned at the PV ostium (not inside the PV) by adjustment of the injection volume (10–12 cc) so the balloon would completely appose the antrum and occlude the PV. The same protocol was followed for each patient, i.e., delivery of a single "shot" of thermal energy to each superior and inferior PV. For wide antral ablation, bilateral upper posterior wall-targeted HBA was performed after the superior PV applications. The balloon was further inflated (14–16 cc) and advanced toward the posterior LA wall or roof at the superior PV antrum level (in close proximity to the superior PV isolation areas) by clockwise or counterclockwise sheath rotation. Subsequently, thermal energy was delivered in a single shot to the right PV carina region (Figure 1). Regardless of the presence or absence of residual conduction, no further HBA was performed.

To prevent phrenic nerve injury, diaphragmatic pacing was performed from electrodes placed along the lateral wall of the superior vena cava. To avoid esophageal damage, esophageal temperature monitoring was

performed with a steerable esophageal temperature probe (Esophastar, Japan Lifeline, Tokyo, Japan). If the temperature exceeded 39degC, water was injected to cool the esophagus.[1,4,5]

## CBA

CBA was performed with a second-generation cryoballoon system (Arctic Front Advance [ARC-Adv-CB], Medtronic, Minneapolis, MN), as previously described.[6] A 28-mm cryoballoon, used in conjunction with an inner lumen mapping catheter (Achieve, Medtronic), was inflated and advanced to each PV orifice. Once optimal PV occlusion, assessed by contrast angiography, was achieved, cryothermal energy was applied in a single shot to the LSPV for 180–240 seconds and to the other PVs for 180 seconds each (Figure 1). As in HBA, diaphragmatic pacing, and esophageal temperature were monitored. Cryothermal energy application was abandoned when the esophageal temperature reached <20degC.

## Voltage mapping and measurements of the isolated surface area

If the patient was in AF rhythm after ablation, cardioversion was performed. High-density bipolar voltage mapping was performed during sinus rhythm. Bipolar signals were acquired with a 20-pole circular catheter (A Focus-II, Abbott). If necessary, coronary pacing was used to determine the local electrocardiogram. Exit block was confirmed by sequential pacing from the circular catheter. If and where residual PV potentials, manifesting as spontaneous PV reconnections, were seen, touch-up RF ablation was performed at those sites with a 4-mm-tip irrigation catheter (FlexAbility, Abbott). RF energy was applied point-by-point at a maximum power output of 25–35 W, and the temperature was set to a maximum of 43degC.

After confirmation of complete PVI, as shown in Figure 2, the isolated antral surface area (IASA) and posterior LA wall surface area were measured by means of the NavX system. The PV ostium was identified as the point of maximal inflection between the PV wall and LA wall, and the PV antrum was defined as the region proximal to the PV ostium. An IASA was defined as an area on the NavX map between an area of low voltage (<0.2 mV) and the corresponding PV ostium (Figure 2),[7] and the sum of the right-sided and left-sided IASAs was taken as the total IASA. The posterior LA wall surface area was defined as the area formed by the superior and inferior margins of the LA and the section of posterior LA wall with bipolar voltage amplitudes of >0.2 mV. The ratio of the total IASA, excluding the PVs, to the sum of the IASA and PWSA was taken as the isolated surface area (ISA). The ISA (%) was calculated as follows: total IASA [cm2] / (total IASA [cm2] + posterior LA wall surface area [pLAWSA] [cm2]) x100.

## Post-ablation follow-up

On the day after the ablation procedure, all antiarrhythmic drugs previously prescribed were resumed, at the individual operator's discretion. Follow-up was performed at the hospitals' respective outpatient clinics, where physical examination and 12-lead electrocardiography were performed at 2 weeks, and every 1 months thereafter. Twenty-four-hour Holter recordings were obtained at 1,3, and 6 months and every 3 months thereafter. Any symptomatic or documented atrial arrhythmia of [?]30 seconds after a 3-month blanking period was taken as a recurrence of the AF.

## Statistical analysis

Data are shown as mean +- SD or median ($25^{\text{th}}$, $75^{\text{th}}$ percentile) values. Patient's baseline clinical, echocardiographic, and electrophysiologic characteristics were compared between the 2 propensity score-matched groups. Procedure-related details and complications were also compared between the 2 groups. Differences were analyzed by Student $t$ -test, Mann-Whitney $U$ -test, or $\chi^2$ test, as appropriate. All patients were followed up for at least 12 months, Kaplan-Meier curves for the freedom from AF/atrial tachycardia (AT) were generated, and between-group differences were analyzed by log-rank test. Predictors of AF recurrence

were performed using Cox proportional hazards regression models. All statistical analyses were performed with JMP 13.2.1 software (SAS Institute, Cary, NC), and $P < 0.05$ was considered significant.

# RESULTS

## Patients' clinical and echocardiographic characteristics

Patients' clinical and echocardiographic characteristics are shown per group in Table 1. The mean duration of AF was 6 months, and mean LAD was 41 mm in both groups. Only the type of AADs used was found to differ significantly between the 2 groups, with Class III or IV AADs given more frequently to patients in the CBA group than to patients in the HBA group.

## Patients' electrophysiologic characteristics and details of the ablation procedures

Patients' electrophysiologic characteristics and the procedure-related details are shown per group in Table 2. Complete PVI was achieved in all cases. AF termination occurred significantly less frequently during HBA than during CBA (19 [24%] vs. 31 [39%], $P = 0.04$). The energy application times were equivalent for the superior PVs, but for the inferior PVs, the energy application time was shorter in the HBA group than in the CBA group (LIPV: 145 ± 17 vs. 162 ± 28 seconds,$P < 0.001$; RIPV: 145 ± 17 vs. 162 ± 28 seconds,$P$ <0.001). Touch-up RF applications were required to complete the PVI in 15 (19%) patients in the HBA group and 12 patients (15%) in the CBA group ($P = 0.52$), and a significant between-group difference was found in some sites requiring touch-up, with energy applications needed at the LSPV in 12 (15%) patients in the HBA group and at the RIPV in 5 (6%) patients in the CBA group. CTI ablation was performed significantly more often after CBA than after HBA (32 [41%] vs. 9 [11%], $P < 0.001$). No patient received additional LA substrate ablation targeting fractionated electrograms or low-voltage areas. There was no significant between-group difference in the procedure time.

## ISAs

Representative voltage maps displaying ISAs achieved by HBA and by CBA are shown in Figure 3. As shown in Table 2, the total IASA + pLAWSA did not differ significantly between the HBA group and CBA group (42.2 ± 9.5 $cm^2$ vs. 42.5 ± 11.5 $cm^2$, $P = 0.83$). However, the total IASA after HBA was significantly larger than that after CBA (26.3 ± 11.0 $cm^2$ vs. 21.4 ± 7.0 $cm^2$, $P < 0.001$). Thus, the ISA after HBA was greater than that after CBA (61 ± 16% vs. 51 ± 12%, $P< 0.001$). Distribution of the ISAs resulting from each of the balloon systems is shown in Figure 4.

## Complications

Periprocedural complications are shown per group in Table 3. The number of patients who suffered a complication did not differ significantly between the HBA group and CBA group (3 [4%] vs. 1 [1%],$P = 0.62$). Pericardial tamponade, pericarditis, and aspiration pneumonia occurred in 1 patient each in the HBA group, but all 3 patients recovered within 2 weeks after the procedure. Phrenic nerve paralysis occurred in 1 patient in the CBA group, and this resolved within 2 months after the procedure. There was no periprocedural death in either group.

## Post-ablation antiarrhythmic therapies and outcomes, per study group

Post-ablation antiarrhythmic therapies and outcomes are shown in Table 4. Twenty-four (30%) HBA and 34 (43%) CBA patients were given 1 or more AADs after the procedure ($P = 0.10$). There was no between-group difference in the number of patients given a class I drug (2 [3%] vs. 7 [9%], respectively; $P = 0.17$), class

III (amiodarone) drug (4 [5%] vs. 1 [1%], respectively; $P = 0.17$), or class IV (bepridil) drug (20 [25%] vs. 29 [37%], respectively; $P = 0.12$). beta-blockers were given to more patients in the CBA group than in the HBA group (23 [29%] vs. 6 [8%], respectively; $P < 0.001$).

During the median follow-up period of 18 (13, 26) months, 8 patients (10%) in the HBA group and 12 patients (15%) in the CBA group experienced AF recurrence ($P = 0.34$). Atrial tachycardia (AT) was observed in 1 patient (1%) in the HBA group and 2 patients (3%) in the CBA group. Kaplan-Meier curves for freedom from AF/AT recurrence are shown in Figure 5. Freedom from AF/AT recurrence was similar between patients who underwent HBA and those who underwent CBA ($P = 0.69$). AF/AT recurrence did not differ statistically between the HBA group and CBA group during the during the first 18 months after the procedure (11% vs. 18%, respectively, at 18 months; $P = 0.26$). None of the clinical or procedure-related variables were found to predict AF recurrence.

# DISCUSSION

To the best of our knowledge, this is the first reported study to compare the clinical efficacy and safety of HBA and CBA performed for PerAF. The study was conducted on a propensity score-match sample, and the isolation areas were carefully evaluated by high-resolution mapping. Our two main findings were as follows: (1) The isolation areas produced by HBA and by CBA were generally wide, but those produced by HBA were significantly larger than those produced by CBA, although additional energy applications were needed when HBA was performed. (2) The procedural safety and the clinical efficacy shown at 18 months were comparable between the 2 balloon systems.

## Isolation areas created by the 2 balloon systems

Recently, a single "big balloon" technique has become a standard CBA technique because the large freezing surface of the second-generation cryoballoon allows for coverage of both small and large PVs as well as creation of antral lesion sets.[8] Our study findings are in line with those of a previously reported study showing that the lesion created by the cryoballoon was relatively large.[9] Miyazaki et al. reported that the isolation area ratio at the LSPV antrum was significantly smaller in patients with a funnel-shaped or common left PV than in others.[10] This may be attributable to the spherical nature of the cryoballoon and size mismatch of the balloon to the PV orifice, suggesting that the area covered by the cryoballoon depends highly on the patient's LA anatomy. Anatomical factors might have affected our patients only slightly, if at all; our study included only patients with AF of relatively short duration (average: 6 months) and minimal LA remodeling (average LAD: 41 mm).

Unique to HBA is the fact that the balloon remains compliant even during energy delivery; the cryoballoon stiffens during energy delivery. However, the hot balloon often yields a relatively small ablation area because this type of balloon tends to inside the PV orifice[1]. Results of reported studies have indicated that larger PV antral isolation and LA posterior wall isolation areas improve clinical outcomes for patients with PerAF.[11,12]Further, feasibility of cryoballoon-based linear ablation along the LA roof and/or floor has been demonstrated recently.[13,14]On the basis of these reported findings, we employed additional upper posterior wall energy application to create a larger ablation area and so reduce the risk of recurrence. As a result, our HBA protocol yielded a wider antral isolation area than that of the standard CBA protocol. Notably, the balloon can be adjusted to fit the antral region, regardless of its size, including part of the posterior wall because it is highly compliant. Further, since HBA is performed under temperature control, it allows for stable lesion creation without complete occlusion of the PV even when the balloon is positioned near the LA antrum. Thus, the hot balloon appears be particularly suitable for creation of a wide planar antral isolation area in patients with PerAF. Additional studies are needed to further establish the validity of the approach.

## Efficacy of the 2 balloon systems for PerAF

CBA-based antral PVI has been shown to be efficacious in patients with paroxysmal AF, and the 84–93% 1-year success rates have been reported after performance of PVI by HBA in such patients.[1,15,16]Several groups of investigators have compared antral PVI performed by CBA or by contact force-guided RF ablation in patients with paroxysmal AF [17] and those with PerAF,[3] but there are no comparative data regarding clinical outcomes of PVI performed by HBA in patients with PerAF. Although recent reports have documented 1-year procedural success rates as high as 76–79%,[18,19]ablation for PerAF remains challenging. Our study revealed good clinical outcomes, whether by HBA or by CBA. One possible explanation for the improved outcome is that our cohort consisted of patients with relatively early-phase PerAF and a minimally remodeled LA. A wide and sufficient ablation region might have been created easily in these patients. Another possible explanation is that nearly a third of the patients were on AAD therapy even during the follow-up period. Nonetheless, the high success rates of both balloon modalities may be due to durable PVI and partial modification of the LA substrate resulting from the wide ablation areas. Randomized studies are warranted to elucidate the clinical efficacy of each of the 2 balloon systems.

## Procedural safety and complications

The incidence of complications among our study patients did not differ significantly from previously reported incidences.[6,14,15,20]A multicenter randomized study has already revealed the safety of the hot balloon system.[4]Basically, myocardial tissue is ablated by conductive heating from the balloon surface via agitated fluid, which is warmed by Joule heating derived from coil electrodes within the balloon. Thus, the tissue temperature will be highest at the site were the balloon contacts the endocardial tissue surface, and the temperature will gradually decrease at deeper levels. Thus, the hot balloon poses a low risk for an abnormal rise in temperature inside the tissue, and this may prevent both thrombus formation and steam pops.

When LIPV-targeted HBA was performed, the esophageal temperature tended to rise due to placement of the balloon in close proximity to the esophagus. To avoid esophageal complications, we applied an active esophageal cooling protocol by injecting cooled saline during the energy delivery.[5] This resulted in aspiration pneumonia in 1 of our patients, Although rare, care should be taken to avoid this complication during HBA. Phrenic nerve injury (PNI) is of major concern during CBA.[6,21]PNI occurred in 1 of our patients during CBA, and no PNI was observed during HBA. The reported incidence of PNI during HBA for paroxysmal AF is 0–3.7%,[4,15]and additional PV antrum application did not significantly affect the occurrence of PNI. We found additional extra PV ostial application during HBA for PerAF to be as safe as reported previously.

## Study limitations

Because our study was conducted as a dual-center study that involved a relatively small number of patients with PerAF, our findings should be confirmed by further studies. Also, asymptomatic episodes might have been underestimated because the AF recurrence rate was evaluated only on the basis of spot electrocardiograms obtained during patients' follow-up visits or by and Holter monitoring. Our study results should be interpreted cautiously because the patients were not randomized to treatment. The patients were matched on the basis of propensity scores, but unknown clinical characteristics or anatomical considerations that might have affected the outcomes could not be ruled out.

# CONCLUSIONS

Although the HBA and CBA protocols differed, and the lesions to which each of these 2 ablation systems were applied also differed, HBA and CBA were shown to be comparable in terms of the wide antral regions isolated, clinical efficacy, and safety when used for patients with PerAF.

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**TABLE 1** Patients' clinical and echocardiographic characteristics, per study group

| | HBA (n = 79) | CBA (n = 79) | *P* value |
|---|---|---|---|
| Clinical characteristics | | | |
| Age (years) | 64 ± 9 | 64 ± 10 | 0.98 |
| Male sex | 60 (76%) | 62 (78%) | 0.70 |
| BMI (kg/m$^2$) | 25 ± 4 | 25 ± 4 | 0.93 |
| AF duration (months) | 6 ± 2 | 6 ± 3 | 0.61 |
| AF lasting < 3 months | 6 (8%) | 12 (15%) | 0.13 |
| 3-6 months | 27 (34%) | 28 (35%) | 0.87 |
| 6-12 months | 46 (58%) | 39 (49%) | 0.26 |
| $CHA_2DS_2$-VASc score | 2 (1, 3) | 2 (1, 3) | 1.00 |
| Heart failure | 12 (15%) | 10 (13%) | 0.65 |
| Hypertension | 39 (49%) | 45 (57%) | 0.34 |
| Diabetes mellitus | 11 (14%) | 15 (19%) | 0.39 |
| Prior stroke | 11 (14%) | 8 (10%) | 0.46 |
| Vascular disease | 6 (8%) | 3 (4%) | 0.49 |
| Antiarrhythmic drug use | 52 (66%) | 54 (68%) | 0.73 |
| Class I | 10 (13%) | 14 (18%) | 0.37 |
| Class III or IV | 12 (9%) | 32 (38%) | <0.001 |
| β blocker | 44 (56%) | 29 (37%) | 0.02 |
| Anticoagulant drug use | 79 (100%) | 79 (100%) | 1.00 |
| Warfarin | 2 (3%) | 3 (4%) | 1.00 |
| DOAC | 77 (97%) | 76 (96%) | 1.00 |
| Echocardiographic variables | | | |
| LVEF (%) | 62 ± 13 | 62 ± 11 | 0.84 |
| LAD (mm) | 41 ± 6 | 41 ± 5 | 0.80 |

Mean ± SD or median ($25^{th}$, $75^{th}$percentile) values or number (%) of patients are shown.

AF = atrial fibrillation; BMI = body mass index; CBA = cryoballoon ablation; DOAC = direct oral an-

ticoagulant; HBA = hot balloon ablation; LAD = left atrial diameter; LVEF = left ventricular ejection fraction.

**TABLE 2** Electrophysiologic characteristics and procedure-related details, per study group

| | HBA (n = 79) | CBA (n = 79) | *P* value |
|---|---|---|---|
| Baseline rhythm is AF | 79 (100%) | 79 (100%) | - |
| Termination of AF during PVI | 19 (24%) | 31 (39%) | 0.04 |
| Amount of fluid injected into hot balloon (mL) | | | |
| LSPV | 11.7 ± 1.6 | - | - |
| Left upper aspect of the posterior LA wall | 14.2 ± 1.7 | - | - |
| LIPV | 11.6 ± 1.5 | - | - |
| RSPV | 11.7 ± 1.3 | - | - |
| Right upper aspect of the posterior LA wall | 13.4 ± 1.6 | - | - |
| RIPV | 11.1 ± 1.5 | - | - |
| Energy application time (seconds) | | | |
| LSPV | 185 ± 33 | 191 ± 32 | 0.21 |
| Left upper aspect of the posterior LA wall | 145 ± 18 | - | - |
| LIPV | 145 ± 17 | 162 ± 28 | <0.001 |
| RSPV | 172 ± 26 | 166 ± 27 | 0.17 |
| Right upper aspect of the posterior LA wall | 124 ± 8 | - | - |
| RIPV | 145 ± 13 | 167 ± 27 | <0.001 |
| Touch up ablation | 15 (19%) | 12 (15%) | 0.52 |
| LSPV | 12 (15%) | 2 (3%) | <0.01 |
| LIPV | 0 (0%) | 2 (3%) | 0.16 |
| RSPV | 2 (3%) | 3 (4%) | 0.65 |
| RIPV | 1 (1%) | 5 (6%) | 0.09 |
| CTI ablation | 9 (11%) | 32 (41%) | <0.001 |
| Procedure time (minutes) | 155 ± 35 | 164 ± 60 | 0.22 |
| Fluoroscopy time (minutes) | 45 ± 10 | 37 ± 13 | <0.01 |
| Total mapping points | 2018 ± 692 | 2051 ± 671 | 0.827 |
| Ablation area | | | |
| Total IASA + pLAWSA ($cm^2$) | 42.2 ± 9.5 | 42.5 ± 11.5 | 0.83 |
| Total IASA ($cm^2$) | 26.3 ± 11.0 | 21.4 ± 7.0 | <0.001 |
| ISA (%) | 61 ± 16 | 51 ± 12 | <0.001 |

Mean ± SD values or number (%) of patients are shown.

AF = atrial fibrillation; CBA = cryoballoon ablation; CTI = cavotricuspid isthmus; HBA = hot balloon ablation; IASA= isolated antrum surface area; ISA= isolated surface area; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein; pLAWSA= posterior left atrial wall surface area; PVI = pulmonary vein isolation.

**TABLE 3** Complications during or after the procedure, per study group

| | |
|---|---|
| Total complications | |
| Death | |
| Pericardial tamponade | |
| TIA/stroke | |
| Phrenic nerve injury | |

| | |
|---|---|
| Atrioesophageal fistula | |
| Pericarditis | |
| Aspiration pneumonia | |
| Pseudoaneurysm | |
| Severe PV stenosis | |

Number (%) of patients are shown. CBA = cryoballoon ablation; HBA = hot balloon ablation; PV = pulmonary vein; TIA

**TABLE 4** Antiarrhythmic therapy and AF/AT recurrence during the follow-up, per study group

| | HBA (n =79) | CBA (n = 79) | *P* value |
|---|---|---|---|
| Antiarrhythmic drug use | 24 (30%) | 34 (43%) | 0.10 |
| Class I | 2 (3%) | 7 (9%) | 0.17 |
| Class III or IV | 24 (30%) | 30 (34%) | 0.31 |
| β blocker | 6 (8%) | 23 (29%) | <0.001 |
| AF/AT recurrence | 9 (11%) | 14 (18%) | 0.26 |
| AF recurrence | 8 (10%) | 12 (15%) | 0.34 |
| AT recurrence | 1 (1%) | 2 (3%) | 1.00 |

Number (%) of patients is shown.

AF = atrial fibrillation; AT = atrial tachycardia; CBA = cryoballoon ablation; HBA = hot balloon ablation.

**Figure legends**

**FIGURE 1**

Details of the HBA and CBA technique. The cryoballoon or hotballoon is positioned to include each of the 4 PV antra and the PV-LA junctions. In addition, the HBA is applied to the bilateral upper posterior LA wall and right carina region. CBA = cryoballoon ablation; HBA = hot balloon ablation; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

**FIGURE 2**

A. Pre-operative 3D-CT image. B. Identification of the pulmonary vein ostium (white line) and isolated antral surface area (IASA) (grey area: <0.2mV). C. Total IASA and left atrial posterior wall surface area (PWSA). D. Left-sided IASA and right-sided IASA. IASA total = total IASA.

**FIGURE 3**

Representative voltage maps showing areas of pulmonary vein antrum isolation achieved by CBA and by HBA. The HBA areas are larger than the CBA areas. CBA = cryoballoon ablation; HBA = hot balloon ablation.

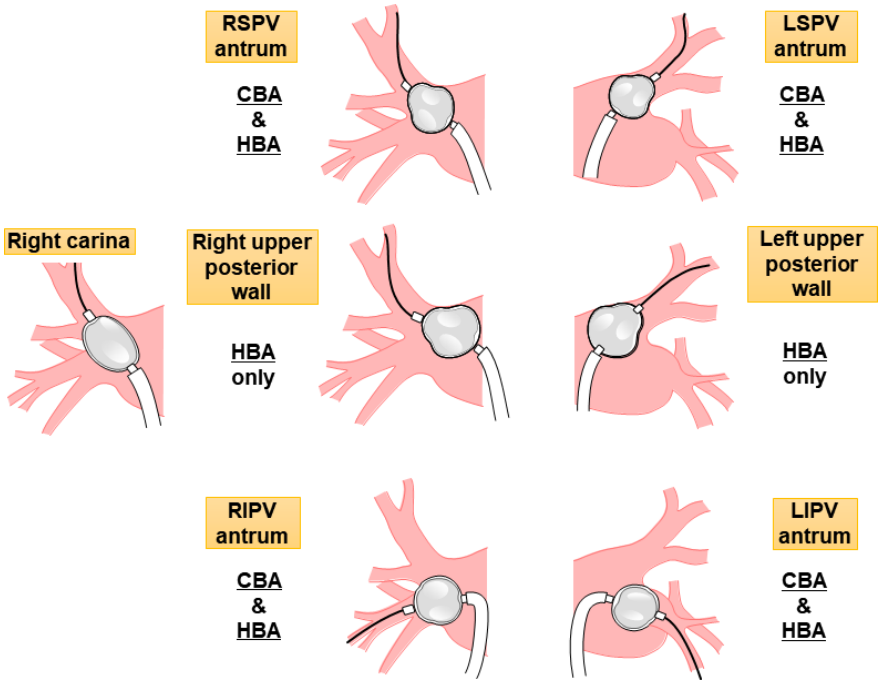
**FIGURE 4**

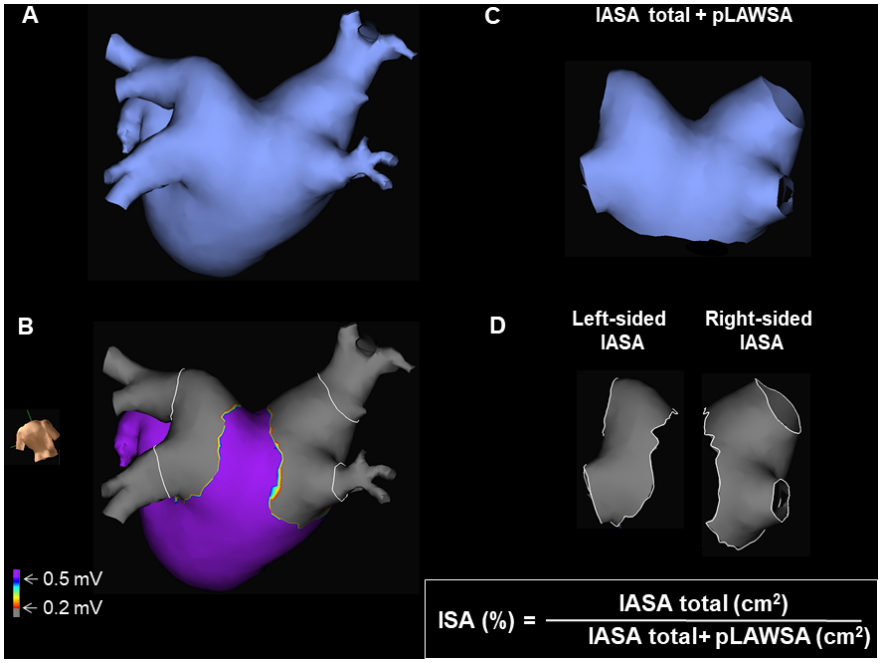
Bar graph showing size and distribution of the isolated surface areas (ISAs) in the HBA group and CBA group.

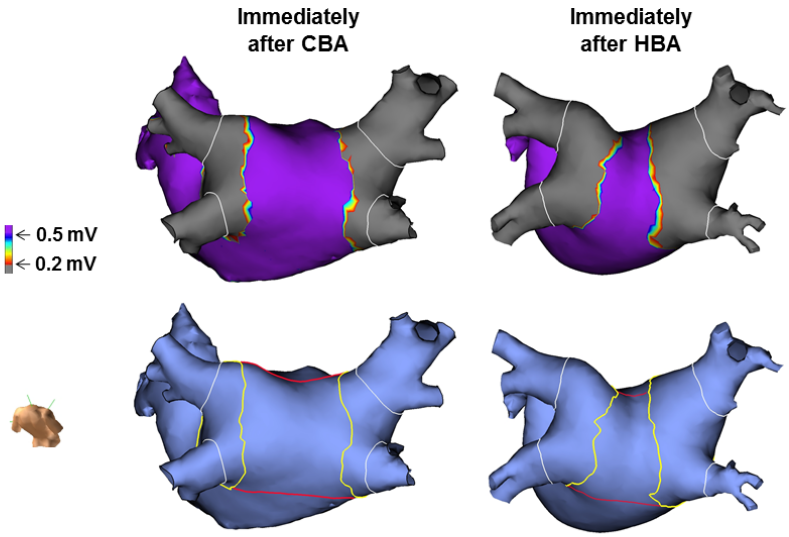
**FIGURE 5**

Kaplan-Meier curves for freedom from AF/AT among patients treated by HBA or CBA for persistent AF.

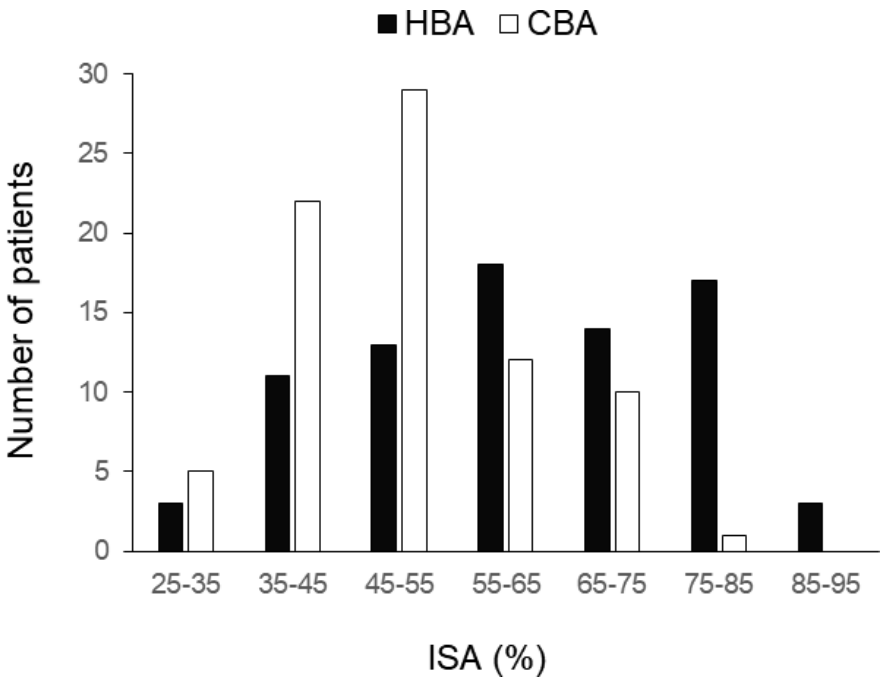
AT = atrial fibrillation; AT = atrial tachycardia.

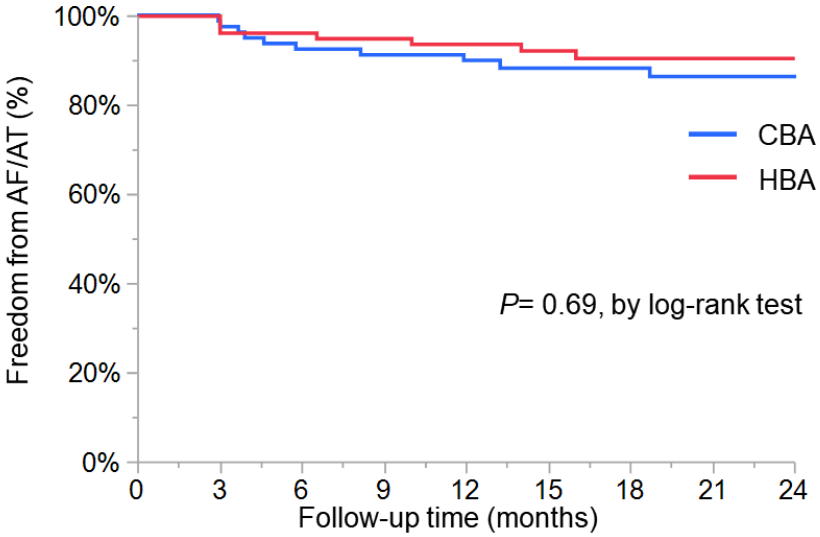





| | | | |
|---|---|---|---|
| **Left-sided IASA ($cm^2$)** | 9.0 | | 14.1 |
| **Right-sided IASA ($cm^2$)** | 10.2 | | 19.2 |
| **IASA total + LAPW surface area ($cm^2$)** | 37.2 | | 43.5 |
| **ISA (%)** | 51.6 | | 76.6 |






Numbers at risk

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| CBA group: | 79 | 79 | 73 | 72 | 71 | 49 | 47 | 43 | 40 |
| HBA group: | 79 | 79 | 76 | 75 | 74 | 58 | 43 | 31 | 24 |