

# Does Sinus Rhythm Restoration in Patients With Atrial Fibrillation Undergoing Pulmonary Vein Isolation Have Acute Hemodynamic Benefits?

Tomo Komaki<sup>a, c</sup>, Noriyuki Mohri<sup>a</sup>, Akihito Ideishi<sup>a</sup>, Kohei Tashiro<sup>a</sup>, Naoko Koyanagi<sup>b</sup>, Shin-ichiro Miura<sup>a</sup>, Masahiro Ogawa<sup>a, b</sup>

## Abstract

**Background:** Although the restoration and maintenance of sinus rhythm (SR) in patients with atrial fibrillation (AF) have long-term benefits, few studies have investigated the acute hemodynamic benefits immediately after SR restoration. Therefore, we investigated whether hemodynamic changes occurred in the first few minutes after cardioversion from AF to SR.

**Methods:** We retrospectively enrolled 145 patients with AF and divided them into a pre-AF group comprising patients in whom SR was restored by electrical cardioversion during pulmonary vein isolation (PVI;  $n = 74$ ) and a control group comprising patients who were in SR throughout the procedure ( $n = 71$ ). The pre-AF group was subdivided into subgroups according to AF classification (paroxysmal AF (PAF), persistent AF (PerAF), and long-standing persistent AF (LSPAF)) and into quartiles based on the AF-heart rate (HR). The mean arterial pressure (MAP) and left atrial pressure (LAP) were measured immediately after transseptal puncture (pre-measurement) and before withdrawal from the left atrium after PVI (post-measurement). The changes in MAP and LAP between the pre- and post-measurement ( $\Delta$ MAP and  $\Delta$ LAP) were calculated by subtracting the pre-measurements ( $MAP_{pre}$  and  $LAP_{pre}$ ) from the post-measurements ( $MAP_{post}$  and  $LAP_{post}$ ).

**Results:** In the pre-AF group, the time from cardioversion to post-measurement was  $19 \pm 16$  min. When  $\Delta$ MAP and  $\Delta$ LAP were compared with the control group,  $\Delta$ MAP was significantly smaller ( $4.9 \pm 17.8$  vs.  $11.0 \pm 14.2$  mm Hg, respectively;  $P = 0.025$ ), and  $\Delta$ LAP was not significantly different between the groups. In the subgroup analyses, although  $\Delta$ LAP was not significantly different among AF types,  $\Delta$ MAP was significantly increased in the PAF group compared to the PerAF and LSPAF groups ( $24.0 \pm 18.5$  vs.  $3.1 \pm 16.8$  and  $4.5 \pm 18.1$  mm

Hg, respectively;  $P = 0.042$ ). The  $HR_{pre}$  in the quartiles with the lowest, second, third, and highest AF-HR were approximately 58, 74, 86, and 109 beats per minute (bpm), respectively. The  $\Delta$ LAP and  $\Delta$ MAP were not significantly different among the AF-HR quartile groups.

**Conclusions:** In patients with PAF, atrial contractions may resume quickly, which leads to hemodynamic improvement immediately after SR restoration. As for AF-HR, there was no significant impairment of ventricular diastolic filling at approximately  $< 109$  bpm.

**Keywords:** Atrial fibrillation; Cardioversion; Mean arterial pressure; Left atrial pressure; Sinus rhythm

## Introduction

Atrial contraction pumps blood into the ventricles, leading to increments in ventricular diastolic and stroke volumes [1, 2]. Atrial fibrillation (AF) decreases atrial contraction and can therefore reduce the stroke volume. Most researchers agree that loss of atrial contraction reduces cardiac output by 20% [3]. This effect may be particularly important in patients with reduced left ventricular compliance such as those with hypertrophic cardiomyopathy [4]. AF also causes an irregular rhythm and decreases the cycle length in a rapid ventricular response, which impairs optimal ventricular diastolic filling and reduces the stroke volume [5]. Uncontrolled persistent tachycardia can lead to a decrease in cardiac output and rate-related atrial and/or ventricular cardiomyopathy [6, 7]. These factors may contribute to adverse hemodynamic changes in patients with AF.

Cardioversion from AF to sinus rhythm (SR) optimizes ventricular diastolic filling because atrial contraction resumes and the cycle length increases, resulting in improved cardiac output [8, 9]. If SR can be maintained for a long period in patients with AF, it can stabilize neurohumoral activation and improve mitral regurgitation by decreasing the left atrial diameter and ventricular function, especially in patients with tachycardia-induced cardiomyopathy [10-12]. Rhythm control is very effective in improving symptoms and cardiac function in AF; therefore, the Japanese Circulation Society/Japanese Heart Rhythm Society 2021 guideline recommends catheter

Manuscript submitted June 27, 2024, accepted August 12, 2024

Published online August 20, 2024

<sup>a</sup>Department of Cardiology, Fukuoka University Hospital, Fukuoka, Japan

<sup>b</sup>Department of Clinical Laboratory Medicine, Fukuoka University Faculty of Medicine, Fukuoka, Japan

<sup>c</sup>Corresponding Author: Tomo Komaki, Department of Cardiology, Fukuoka University Hospital, Fukuoka 814-0180, Japan.

Email: tomokomaki1981@yahoo.co.jp

doi: <https://doi.org/10.14740/cr1692>

ablation for patients with AF and heart failure (recommendation class II a) [13-15].

To date, few studies have investigated the acute effects of cardioversion from AF to SR. We were interested in evaluating the changes in mean arterial pressure (MAP), as a surrogate marker for cardiac output, and left atrial pressure (LAP) immediately after restoration of SR. Therefore, we studied patients with AF who underwent pulmonary vein isolation (PVI) by radiofrequency catheter ablation (RFCA) in our hospital and investigated the acute hemodynamic effects by measuring the blood pressure, including the MAP and LAP, before and after cardioversion.

## Materials and Methods

### Study population

This retrospective, observational study included 145 consecutive patients with AF who underwent PVI by RFCA. The patients were enrolled at Fukuoka University Hospital, Fukuoka, Japan, between August 2019 and April 2023. Patients with drug-refractory AF, aged  $\geq 18$  years were included. Exclusion criteria were as follows: 1) additional intra-left atrial linear ablation and/or ablation of non-pulmonary vein triggers beyond PVI; 2) inadequate LAP measurements because of inadequate breath-holding; 3) insufficient perioperative data; 4) severe valvular disease; 5) maintenance hemodialysis for end-stage renal disease; 6) use of beta-agonists and/or adenosine triphosphate as provocative agents after PVI; 7) spontaneous change in heart rhythm from AF to SR or from SR to AF during the procedure; and 8) dependency on cardiac pacing with an implanted pacemaker.

The patients were divided into a pre-AF group, comprising those who had AF at the time they entered the cardiac catheterization laboratory that was reversed to SR by electrical cardioversion during PVI ( $n = 74$ ), and a control group, comprising those who were in SR throughout the PVI procedure ( $n = 71$ ). For subgroup analyses, we subdivided the pre-AF group into subgroups according to AF classification, that is, paroxysmal AF (PAF), persistent AF (PerAF), and long-standing persistent AF (LSPAF) and into quartiles according to the AF-heart rate (HR) and left atrial dimension (LAD). The AF type was determined according to the 2016 European Society of Cardiology guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardiothoracic Surgery [16]. PAF was defined as AF that reversed to SR within 7 days of occurrence, PerAF as AF that persisted for  $> 7$  days after occurrence, and LSPAF as AF that persisted for longer than a year.

### Ethical issues

This study was approved by the Institutional Review Board (U22-08-016) of Fukuoka University Hospital. All procedures of the present study were conducted in compliance with the Helsinki Declaration for research on human beings.

### Clinical parameters

We collected admission data on age; sex; body mass index (BMI); comorbidities, including hypertension and diabetes mellitus; New York Heart Association (NYHA) functional class; laboratory tests, including hemoglobin, creatinine clearance, and B-type natriuretic peptide; and echocardiographic parameters, including LAD, left ventricular ejection fraction (LVEF); and heart failure and antiarrhythmic drugs taken before RFCA. HR and blood pressure, including systolic blood pressure (SBP), diastolic blood pressure (DBP), MAP, and LAP, were recorded twice during PVI; a pre-measurement was made immediately after entering the left atrium (LA) by transseptal puncture, and a post-measurement was made after completion of PVI, immediately before withdrawal from the LA. Data were also collected on the intraoperative amounts of intraprocedural fluid, sedatives (dexmedetomidine, fentanyl, diazepam, and thiopental), and contrast agents (in patients who underwent pulmonary vein angiography). The timing of electrical cardioversion during PVI was at the surgeon's discretion and the time from cardioversion to post-measurement was recorded in the pre-AF group. The changes in HR and blood pressure between the pre- and post-measurements ( $\Delta$ HR,  $\Delta$ SBP,  $\Delta$ DBP,  $\Delta$ MAP, and  $\Delta$ LAP) were calculated by subtracting the pre-measurements from the post-measurements.

### Anesthesia management

All patients were sedated without intubation and administered oxygen at 2 L/min throughout the procedure under oxygen saturation and invasive blood pressure monitoring. Both diazepam 2.5 - 5 mg and fentanyl 0.05 mg were administered intravenously at the beginning of ablation. Dexmedetomidine was simultaneously administered by continuous infusion at an initial loading dose of 4  $\mu$ g/kg/h over 10 min, followed by a maintenance dose at a rate of 0.4  $\mu$ g/kg/h. The depth of sedation was assessed by the Bispectral Index<sup>®</sup> monitor (Aspect Medical Systems Inc, Natick, MA, USA), with a target value of 60 - 80. Depending on the patient's pain and alertness during the procedure, diazepam and fentanyl were added, and the maintenance dose of dexmedetomidine was adjusted. In the pre-AF group, thiopental was additionally administered at a dose of 1 mg/kg for transient deep sedation immediately before electrical cardioversion.

### RFCA

Antiarrhythmic drugs were discontinued in all patients for at least five half-lives before PVI. All patients underwent circumferential PVI with a ThermoCool<sup>®</sup> Surround Flow catheter (Biosense Webster, Diamond Bar, CA, USA) and the CARTO-3 mapping system (Biosense Webster, Diamond Bar, CA, USA). In this cohort, no additional substrate modifications beyond PVI were performed. In patients with redo AF, only the recurrent pulmonary vein potentials were isolated.

After double transseptal puncture was performed by a radiofrequency needle, an SL-0 sheath (St. Jude Medical, St. Paul, MN, USA) and Agilis™ sheath (St. Jude Medical, St. Paul, MN, USA) were inserted into the LA. Pulmonary vein angiography was performed in most patients. Internal cardioversion was performed using a BeeAT catheter (Japan Lifeline, Tokyo, Japan) connected to a dedicated defibrillator (Shock AT; Japan Lifeline, Tokyo, Japan) to restore the SR. External cardioversion was performed in patients in whom the BeeAT catheter could not be placed in the coronary sinus. The timing of electrical cardioversion during PVI was at the surgeon's discretion. During PVI, the pulmonary vein potentials were monitored using a ring catheter and the electrophysiological endpoint was a bidirectional conduction block between the LA and each PV. In patients with common atrial flutter, cavotricuspid isthmus isolation was performed after LA withdrawal during PVI.

### Statistical analysis

Data were analyzed using the Stat Flex software (version 7.0; Artech Co., Ltd., Osaka, Japan). Continuous variables were expressed as mean  $\pm$  standard deviation (SD) or median  $\pm$  quartile deviation, and categorical variables were expressed as percentage (%). Continuous and categorical variables were compared between the two groups using Student's *t*-test and Chi-square tests, respectively. When continuous variables did not show a normal distribution, we performed the Mann-Whitney U test. Continuous and categorical variables were compared among more than three groups by one-way analysis of variance and Chi-square analysis, respectively. When continuous variables did not show a normal distribution, we performed the Kruskal-Wallis test. Statistical significance was set at  $P < 0.05$ .

## Results

### Clinical characteristics in the pre-AF and control groups

In the entire group ( $N = 145$ ), the mean age was  $67 \pm 9$  years, and 102 of the patients (70%) were males. Table 1 shows the clinical characteristics of the pre-AF ( $n = 74$ ) and control ( $n = 71$ ) groups. The BMI was significantly higher in the pre-AF group than in the control group. Comorbidities including hypertension, diabetes mellitus, vascular disease, and stroke were not significantly different between the groups. Heart failure symptoms with NYHA functional class II were significantly more prevalent in the pre-AF group than in the control group. Patients in the pre-AF group had significantly higher hemoglobin and B-type natriuretic peptide levels, greater LAD, and lower LVEF than those in the control group. The uses of heart failure drugs including angiotensin-converting enzyme inhibitors, angiotensin receptor blocker, or angiotensin receptor neprilysin inhibitor, mineralocorticoid receptor antagonist, sodium-glucose cotransporter-2 inhibitor, and loop diuretics were not significantly different between the groups.

Bepridil was used significantly less frequently in the pre-AF group than in the control group. In the entire group, 18% of patients ( $n = 26$ ) were undergoing redo AF ablation; the frequency of redo AF was not significantly different between the groups. Cavotricuspid isthmus ablation for common atrial flutter was performed more frequently in the control group than in the pre-AF group.

### Comparison of intraprocedural parameters between the pre-AF and control groups

Table 2 shows the intra-procedural parameters of both groups.  $HR_{pre}$  was significantly higher in the pre-AF group than in the control group. Compared with the control group, the pre-AF group had significantly lower  $SBP_{pre}$  and higher  $DBP_{pre}$  and  $LAP_{pre}$ . The amounts of intraprocedural fluid and sedatives other than thiopental (dexmedetomidine, fentanyl, and diazepam) administered during PVI were not significantly different between the two groups. Pulmonary vein angiography was performed in 135 patients (pre-AF group,  $n = 67$  (91%); control group,  $n = 67$  (94%)) and the amount of contrast agent used was not significantly different between the two groups. The time from cardioversion to post-measurement was  $19 \pm 16$  min in the pre-AF group. The pre-AF group had significantly lower  $SBP_{post}$  and higher  $LAP_{post}$  than the control group.

### Hemodynamic changes immediately after SR restoration in the pre-AF group

Figure 1a shows the changes in the HR and blood pressure, including SBP, DBP, MAP, and LAP,  $19 \pm 16$  min after cardioversion in the pre-AF group. Immediately after cardioversion, the HR was significantly lower and all blood pressure measurements other than DBP (SBP, MAP, and LAP) were significantly higher.

### Hemodynamic changes after PVI in the control group

Figure 1b shows the changes in HR and blood pressure after PVI in the control group. The HR and all blood pressure measurements (SBP, DBP, MAP, and LAP) were significantly higher after PVI.

### Comparison of the changes in HR ( $\Delta HR$ ) and blood pressure ( $\Delta SBP$ , $\Delta DBP$ , $\Delta MAP$ , and $\Delta LAP$ ) from before to after PVI between the pre-AF and control groups

Figure 2 compares the changes in HR and blood pressure from before to after PVI between the pre-AF and control groups. The pre-AF group showed a significantly greater decrease in HR than the control group ( $\Delta HR$ ,  $-16.3 \pm 18.5$  vs.  $5.9 \pm 9.1$  beats per minute (bpm)), but the changes in SBP and LAP were not significantly different between the two groups. The pre-AF group showed a significantly lower increase in DBP and MAP

**Table 1.** Clinical Characteristics in the Pre-AF and Control Groups

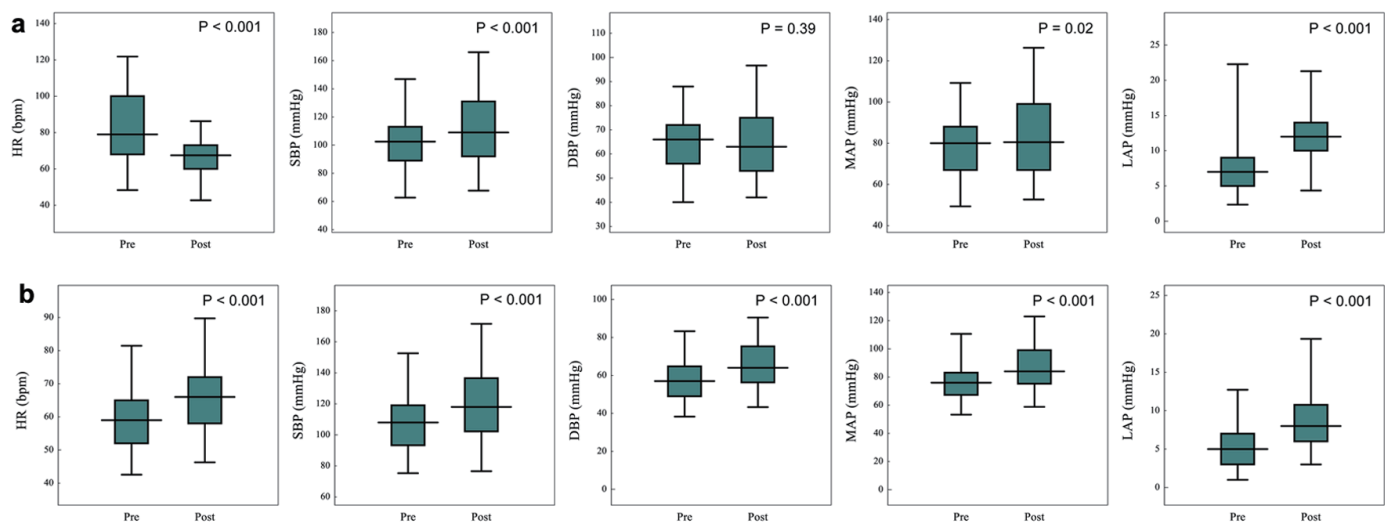
	Pre-AF group (n = 74)	Control group (n = 71)	Pre-AF vs. control P value
Age, years	66 ± 8	67 ± 10	0.44
Male, n (%)	55 (74)	47 (66)	0.28
AF classification			
PAF, n (%)	5 (7)	71 (100)	< 0.001
PerAF, n (%)	48 (65)	0 (0)	< 0.001
LSPAF, n (%)	21 (28)	0 (0)	< 0.001
BMI, kg/m <sup>2</sup>	24.5 ± 3.6	23.3 ± 3.1	0.035
Comorbidities			
HTN, n (%)	45 (61)	44 (62)	0.88
DM, n (%)	12 (16)	6 (9)	0.15
Vascular disease, n (%)	23 (31)	21 (30)	0.84
Stroke, n (%)	8 (11)	5 (7)	0.42
NYHA functional class			
I, n (%)	37 (50)	62 (87)	< 0.001
II, n (%)	37 (50)	9 (13)	< 0.001
Laboratory test			
Hb, g/dL	14.4 ± 1.3	13.5 ± 1.6	< 0.001
CCr, mL/min	76.8 ± 23.6	75.5 ± 23.6	0.74
BNP, pg/mL	179.1 ± 71.8	58.0 ± 47.6	< 0.001
Echocardiographic parameters			
LAD, mm	44.0 ± 5.6	39.5 ± 6.4	< 0.001
LVDD, mm	46.4 ± 5.8	45.8 ± 4.8	0.46
LVDs, mm	31.4 ± 6.2	29.4 ± 6.4	0.059
LVEF, %	59.3 ± 9.6	64.6 ± 9.2	0.001
LVWT, mm	9.7 ± 1.4	9.4 ± 1.8	0.27
Medications			
Heart failure drugs			
ACEI/ARB, n (%)	27 (37)	32 (45)	0.29
ARNI, n (%)	4 (5)	2 (3)	0.43
MRA, n (%)	9 (12)	9 (13)	0.93
SGLT2i, n (%)	7 (10)	5 (7)	0.6
Loop diuretics, n (%)	18 (24)	12 (13)	0.27
AADs			
Class I AADs, n (%)	5 (7)	9 (13)	0.22
Amiodarone, n (%)	1 (1)	4 (6)	0.15
Bepidil, n (%)	16 (22)	28 (39)	0.019
β-blockers, n (%)	49 (66)	42 (59)	0.37
Others, n (%)	6 (8)	3 (4)	0.33
Redo AF ablation, n (%)	13 (18)	13 (18)	0.9
CTI ablation, n (%)	3 (4)	24 (34)	< 0.001

AADs: anti-arrhythmic drugs; ACEI: angiotensin-converting enzyme inhibitors; AF: atrial fibrillation; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor neprilysin inhibitor; BMI: body mass index; BNP: brain natriuretic peptide; CCr: creatinine clearance; CTI: cavotricuspid isthmus; DM: diabetes mellitus; Hb: hemoglobin; HTN: hypertension; LAD: left atrial dimension; LSPAF: long-standing persistent atrial fibrillation; LVDD: left ventricular end-diastolic dimension; LVDs: left ventricular end-systolic dimension; LVEF: left ventricular ejection fraction; LVWT: left ventricular wall thickness; MRA: mineralocorticoid receptor antagonist; NYHA: New York Heart Association; PAF: paroxysmal atrial fibrillation; PerAF: persistent atrial fibrillation; SGLT2i: sodium-glucose cotransporter-2 inhibitor.

**Table 2.** Comparison of Intra-procedural Parameters Between the Pre-AF and Control Groups

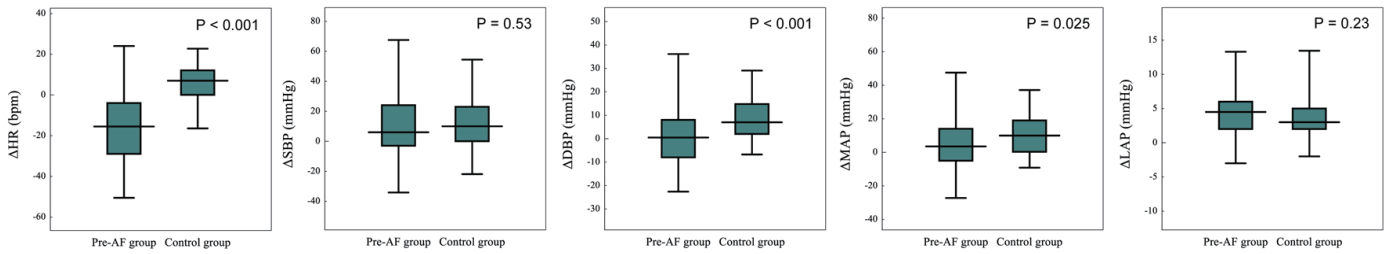
	Pre-AF group (n = 74)	Control group (n = 71)	Pre-AF vs. control P value
<b>Pre-measurement</b>			
HR <sub>pre</sub> , bpm	82.5 ± 20.2	59.7 ± 9.9	< 0.001
SBP <sub>pre</sub> , mm Hg	100.8 ± 21.5	108.5 ± 20.7	0.029
DBP <sub>pre</sub> , mm Hg	64.4 ± 12.9	56.5 ± 12.5	< 0.001
MAP <sub>pre</sub> , mm Hg	78.7 ± 15.8	76.5 ± 16.3	0.39
LAP <sub>pre</sub> , mm Hg	7.9 ± 4.4	5.3 ± 3.3	< 0.001
<b>Intra-procedural comparison</b>			
Total infusion, mL	1,120.6 ± 420.2	999.7 ± 379.6	0.071
<b>Sedatives</b>			
Dexmedetomidine, µg	73.8 ± 25.2	74.8 ± 37.2	0.84
Fentanyl, mg	0.16 ± 0.05	0.17 ± 0.06	0.26
Diazepam, mg	8.4 ± 3.5	9.1 ± 4.5	0.32
Thiopental, mg	90.1 ± 41.8	N/A	N/A
Contrast agent, mL	28.1 ± 11.6	28.2 ± 9.9	0.96
The time after SR restoration, min	18.5 ± 15.5	N/A	N/A
Procedure time, min	168.3 ± 46.4	159.5 ± 52.3	0.29
<b>Post-measurement</b>			
HR <sub>post</sub> , bpm	66.2 ± 10.7	65.6 ± 10.9	0.71
SBP <sub>post</sub> , mm Hg	110.7 ± 26.0	120.6 ± 24.5	0.019
DBP <sub>post</sub> , mm Hg	65.7 ± 15.0	65.3 ± 13.0	0.86
MAP <sub>post</sub> , mm Hg	83.7 ± 19.4	87.4 ± 16.7	0.21
LAP <sub>post</sub> , mm Hg	12.1 ± 4.0	8.8 ± 3.9	< 0.001

AF: atrial fibrillation; DBP: diastolic blood pressure; HR: heart rate; LAP: left atrial pressure; MAP: mean arterial pressure; N/A: not applicable; SBP: systolic blood pressure; SR: sinus rhythm.



**Figure 1.** Changes in heart rate and blood pressure from before to 19 ± 16 min after sinus rhythm restoration in the pre-atrial fibrillation group (a) and from before to after pulmonary vein isolation in the control group (b). AF: atrial fibrillation; bpm: beats per minute; DBP: diastolic blood pressure; HR: heart rate; LAP: left atrial pressure; MAP: mean arterial pressure; SBP: systolic blood pressure.





**Figure 2.** Comparison of the changes in heart rate and blood pressure from before to after pulmonary vein isolation in the pre-atrial fibrillation and control groups. AF: atrial fibrillation; bpm: beats per minute; ΔDBP: change in diastolic blood pressure; ΔHR: change in heart rate; ΔLAP: change in left atrial pressure; ΔMAP: change in mean arterial pressure; ΔSBP: change in systolic blood pressure.

than the control group (ΔDBP, 1.3 ± 13.4 vs. 8.8 ± 9.6 mm Hg; ΔMAP, 4.9 ± 17.8 vs. 11.0 ± 14.2 mm Hg).

**Comparison between the PAF, PerAF, and LSPAF groups**

Table 3 shows the intraoperative parameters in the PAF (n = 5), PerAF (n = 48), and LSPAF (n = 21) groups. The mean dura-

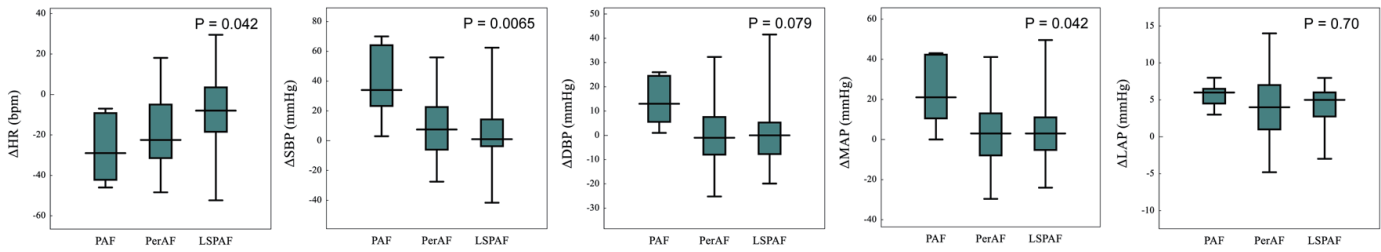
tion of AF in the PAF group was 49.4 ± 34.7 h. The PAF group had a significantly higher HR<sub>pre</sub> and lower SBP<sub>pre</sub>, DBP<sub>pre</sub>, and MAP<sub>pre</sub> than the PerAF and LSPAF groups. The amounts of intraprocedural fluid, sedatives, and contrast agents administered during PVI were not significantly different between the three groups. The HR<sub>post</sub>, SBP<sub>post</sub>, DBP<sub>post</sub>, MAP<sub>post</sub>, and LAP<sub>post</sub> were not significantly different between the three groups.

Figure 3 shows a comparison of the changes in HR and

**Table 3.** Comparison of Intraoperative Parameters Among the AF Classification Groups

	PAF group (n = 5)	PerAF group (n = 48)	LSPAF group (n = 21)	PAF vs. PerAF vs. LSPAF P value
<b>Pre-measurement</b>				
HR <sub>pre</sub> , bpm	93.4 ± 38.3	85.4 ± 19.8	73.4 ± 11.8	0.033
SBP <sub>pre</sub> , mm Hg	73.6 ± 15.8	101.9 ± 20.7	104.8 ± 20.6	0.0099
DBP <sub>pre</sub> , mm Hg	48.2 ± 11.5	65.6 ± 12.5	65.5 ± 11.8	0.012
MAP <sub>pre</sub> , mm Hg	59.6 ± 13.1	80.2 ± 15.6	80.0 ± 14.5	0.017
LAP <sub>pre</sub> , mm Hg	6.2 ± 3.0	8.0 ± 4.9	8.0 ± 3.3	0.67
<b>Intraoperative comparison</b>				
Total infusion, mL	1,283.2 ± 544.4	1,107.2 ± 418.3	1,112.5 ± 408.6	0.67
<b>Sedatives</b>				
Dexmedetomidine, µg	77.6 ± 29.3	70.0 ± 25.5	81.4 ± 22.8	0.21
Fentanyl, mg	0.14 ± 0.065	0.16 ± 0.047	0.186 ± 0.064	0.21
Diazepam, mg	7.0 ± 2.0	8.4 ± 3.8	8.9 ± 3.0	0.54
Thiopental, mg	115.0 ± 57.6	87.5 ± 38.9	91.7 ± 44.3	0.375
Contrast agent, mL	29.4 ± 6.3	29.1 ± 11.5	25.6 ± 12.7	0.5
Procedure time, min	177.2 ± 57.7	165.2 ± 45.1	173.1 ± 48.4	0.73
The time after SR restoration, min	10.0 ± 6.3	21.5 ± 15.5	17.0 ± 8.1	0.29
<b>Post-measurement</b>				
HR <sub>post</sub> , bpm	66.8 ± 21.3	66.6 ± 9.6	65.1 ± 10.4	0.85
SBP <sub>post</sub> , mm Hg	113.4 ± 28.5	110.7 ± 26.6	110.1 ± 25.1	0.96
DBP <sub>post</sub> , mm Hg	62.4 ± 17.3	65.6 ± 13.7	66.8 ± 17.8	0.84
MAP <sub>post</sub> , mm Hg	83.6 ± 23.1	83.2 ± 18.8	84.5 ± 20.7	0.97
LAP <sub>post</sub> , mm Hg	11.8 ± 2.0	12.1 ± 4.7	12.1 ± 2.4	0.98

DBP: diastolic blood pressure; HR: heart rate; LAP: left atrial pressure; LSPAF: long-standing persistent atrial fibrillation; MAP: mean arterial pressure; PAF: paroxysmal atrial fibrillation; PerAF: persistent atrial fibrillation; SBP: systolic blood pressure; SR: sinus rhythm.



**Figure 3.** Comparison of changes in heart rate and blood pressure from before to after pulmonary vein isolation in patients with paroxysmal, persistent, and long-standing persistent atrial fibrillation. bpm: beats per minute; ΔDBP: change in diastolic blood pressure; ΔHR: change in heart rate; ΔLAP: change in left atrial pressure; LSPAF: long-standing persistent atrial fibrillation; ΔMAP: change in mean arterial pressure; PAF: paroxysmal atrial fibrillation; PerAF: persistent atrial fibrillation; ΔSBP: change in systolic blood pressure.

blood pressure before and after PVI in the three groups. The PAF group showed a significantly greater decrease in HR (ΔHR,  $-26.6 \pm 17.7$  bpm) and increases in SBP (ΔSBP,  $39.8 \pm 26.9$  mm Hg) and MAP (ΔMAP,  $24.0 \pm 18.5$  mm Hg) than the PerAF and LSPAF groups.

**Comparison among the AF-HR quartiles in the pre-AF group**

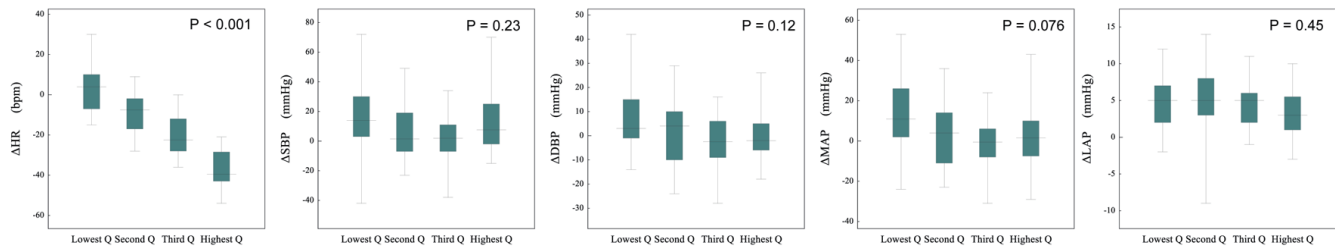
Table 4 shows the intraprocedural parameters among the AF-

HR quartile groups. The HR<sub>pre</sub> in the quartile with the lowest, second, third, and highest AF-HR were  $57.7 \pm 7.4$ ,  $74.0 \pm 2.9$ ,  $86.1 \pm 6.0$ , and  $109.3 \pm 8.1$  bpm, respectively. None of the blood pressure parameters, including the SBP<sub>pre</sub>, DBP<sub>pre</sub>, MAP<sub>pre</sub>, or LAP<sub>pre</sub> were significantly different among the AF-HR quartiles. The amount of fentanyl used during the procedure differed significantly, but there were no significant differences in the amounts of other sedatives, contrast agents, or intraprocedural fluids among the AF-HR quartiles. The HR<sub>post</sub> differed significantly, but all blood pressures, including the

**Table 4.** Comparison of Intraprocedural Parameters Among the Quartile AF-HR Groups

	Lowest Q (n = 18)	Second Q (n = 18)	Third Q (n = 18)	Highest Q (n = 20)	P value
<b>Pre-measurement</b>					
HR <sub>pre</sub> , bpm	$57.7 \pm 7.4$	$74.0 \pm 2.9$	$86.1 \pm 6.0$	$109.3 \pm 8.1$	< 0.001
SBP <sub>pre</sub> , mm Hg	$102.9 \pm 21.7$	$107.9 \pm 23.3$	$96.2 \pm 19.1$	$96.8 \pm 21.2$	0.3
DBP <sub>pre</sub> , mm Hg	$60.7 \pm 14.6$	$64.9 \pm 12.6$	$65.3 \pm 12.0$	$66.5 \pm 12.5$	0.56
MAP <sub>pre</sub> , mm Hg	$75.1 \pm 15.9$	$82.4 \pm 16.9$	$77.9 \pm 15.2$	$79.5 \pm 15.7$	0.58
LAP <sub>pre</sub> , mm Hg	$7.1 \pm 3.4$	$8.5 \pm 5.1$	$6.6 \pm 3.3$	$9.3 \pm 5.1$	0.2
<b>Intraprocedural comparison</b>					
Total infusion, mL	$1,178.9 \pm 496.4$	$1,150.6 \pm 425.4$	$1,197.8 \pm 373.1$	$971.7 \pm 372.1$	0.32
<b>Sedatives</b>					
Dexmedetomidine, µg	$73.0 \pm 22.0$	$70.2 \pm 23.4$	$82.4 \pm 27.4$	$69.8 \pm 27.3$	0.4
Fentanyl, mg	$0.169 \pm 0.049$	$0.181 \pm 0.055$	$0.181 \pm 0.057$	$0.138 \pm 0.048$	0.039
Diazepam, mg	$8.1 \pm 4.0$	$8.1 \pm 2.6$	$10.0 \pm 4.1$	$7.6 \pm 2.8$	0.19
Thiopental, mg	$95.8 \pm 41.3$	$81.9 \pm 36.2$	$95.8 \pm 46.4$	$88.8 \pm 44.0$	0.72
Contrast agent, mL	$29.8 \pm 6.8$	$30.2 \pm 13.5$	$24.6 \pm 12.8$	$27.9 \pm 12.1$	0.45
Procedure time, min	$187.8 \pm 49.8$	$153.6 \pm 40.8$	$177.8 \pm 44.6$	$155.9 \pm 45.0$	0.064
The time after SR restoration, min	$17.0 \pm 17.5$	$13.5 \pm 8.5$	$20.0 \pm 11.5$	$25.0 \pm 15.8$	0.97
<b>Post-measurement</b>					
HR <sub>post</sub> , bpm	$61.6 \pm 12.2$	$64.4 \pm 9.9$	$66.2 \pm 8.1$	$72.1 \pm 10.1$	0.016
SBP <sub>post</sub> , mm Hg	$120.1 \pm 27.2$	$115.2 \pm 32.7$	$98.5 \pm 17.0$	$109.4 \pm 21.7$	0.072
DBP <sub>post</sub> , mm Hg	$68.2 \pm 18.4$	$66.1 \pm 17.9$	$62.6 \pm 10.8$	$66.1 \pm 12.5$	0.73
MAP <sub>post</sub> , mm Hg	$89.1 \pm 21.6$	$85.8 \pm 23.6$	$77.2 \pm 13.1$	$82.6 \pm 17.3$	0.3
LAP <sub>post</sub> , mm Hg	$11.8 \pm 3.2$	$13.6 \pm 2.7$	$10.4 \pm 3.3$	$12.5 \pm 5.6$	0.12

AF: atrial fibrillation; DBP: diastolic blood pressure; HR: heart rate; LAP: left atrial pressure; MAP: mean arterial pressure; Q: quartile; SBP: systolic blood pressure; SR: sinus rhythm.



**Figure 4.** Comparison of the changes in heart rate and blood pressure from before to after pulmonary vein isolation in patients with the quartiles of atrial fibrillation-heart rate. bpm: beats per minute;  $\Delta$ DBP: change in diastolic blood pressure;  $\Delta$ HR: change in heart rate;  $\Delta$ LAP: change in left atrial pressure;  $\Delta$ MAP: change in mean arterial pressure; Q: quartile;  $\Delta$ SBP: change in systolic blood pressure.

$SBP_{post}$ ,  $DBP_{post}$ ,  $MAP_{post}$ , and  $LAP_{post}$  were not significantly different among the AF-HR quartiles.

Figure 4 compares the changes in HR and blood pressure before and after PVI among the AF-HR quartiles. Although the HR decreased significantly more in the quartile with the highest AF-HR than in the quartile with the lowest, second, and third AF-HR ( $\Delta$ HR;  $-37.2 \pm 9.4$  vs.  $3.8 \pm 12.6$ ,  $-9.6 \pm 10.6$ , and  $-19.9 \pm 10.2$  bpm, respectively), the changes in  $\Delta$ SBP,  $\Delta$ DBP,  $\Delta$ MAP, and  $\Delta$ LAP were not significantly different among the AF-HR quartiles.

### Comparison among the LAD quartiles in the pre-AF group

Table 5 shows the intraprocedural parameters among the LAD quartile groups. The LAD in quartile with the lowest, second, third, and highest LAD were  $37.0 \pm 2.9$ ,  $41.8 \pm 0.8$ ,  $45.2 \pm 1.3$ , and  $51.3 \pm 3.1$  mm, respectively. The  $HR_{pre}$  differed significantly, but there were no significant differences in the blood pressure parameters, including the  $SBP_{pre}$ ,  $DBP_{pre}$ ,  $MAP_{pre}$ , and  $LAP_{pre}$  among the LAD quartiles. There were no significant differences in the amounts of intraprocedural fluids, sedatives, or contrast agent among the LAD quartiles. The  $LAP_{post}$  differed significantly, but the  $HR_{post}$  and the other blood pressures, including the  $SBP_{post}$ ,  $DBP_{post}$ , and  $MAP_{post}$  were not significantly different among the LAD quartiles.

Figure 5 compares the changes in HR and blood pressure before and after PVI among the LAD quartiles. The changes in  $\Delta$ HR,  $\Delta$ SBP,  $\Delta$ DBP,  $\Delta$ MAP, and  $\Delta$ LAP were not significantly different among the LAD quartiles.

## Discussion

We investigated the acute hemodynamic effects of SR restoration in patients with AF. As the MAP is determined by cardiac output and peripheral vascular resistance, we used it as a surrogate marker for cardiac output. We were also interested in the change of LAP immediately after cardioversion from AF to SR.

The main findings in this study were as follows. First, hemodynamics could improve immediately after SR restoration in patients with PAF. Compared the pre-AF group includ-

ing all AF types with the control group, there were no significant differences in the changes of MAP and LAP just after SR restoration. We subdivided the pre-AF group according to AF classification and the mean duration of AF in the PAF group was  $49.4 \pm 34.7$  h, which was relatively short duration. When compared among these groups, there was no significant difference in the change of LAP among the groups, but the PAF group showed a significant increase in MAP than the PerAF and LSPAF groups. As the recovery of atrial mechanical function depends on the duration of AF before cardioversion [17], atrial contractions may resume quickly in short duration of AF. As a result, the hemodynamics of the PAF patients improved immediately after SR restoration, whereas those of the PerAF and LSPAF patients did not improve because atrial contractions had not yet resumed. Second, there was no significant impairment of ventricular diastolic filling when AF-HR was at approximately  $< 109$  bpm. To investigate the hemodynamic effects of AF-HR, we subdivided the pre-AF group into quartiles according to AF-HR. Compared among the AF-HR quartiles, there were no significant hemodynamic differences among these groups. Previously, in the RACE II (Rate control efficacy in permanent atrial fibrillation: a comparison between lenient versus strict rate control II) study, Van Gelder et al compared major cardiovascular events in patients with AF treated by a lenient (resting HR  $< 110$  bpm) or strict rate-control strategy (resting HR  $< 80$  bpm and HR during moderate exercise  $< 110$  bpm) [18]. The group hypothesized that the lenient rate-control strategy might induce or worsen heart failure, but the results showed that the lenient strategy was not inferior to the strict strategy. Although the authors did not explain why the lenient rate-control strategy was non-inferior, our findings suggest that this was because neither rate-control strategy caused significant impairment of ventricular diastolic filling. Lastly, the LAD was also significantly different as well as the proportion of AF types and AF-HR ( $HR_{pre}$ ) in comparison of baseline characteristics between the pre-AF group and the control group. As these factors may become confounding factors in the result, we also subdivided the pre-AF group according to the LAD quartiles. But there were no significant hemodynamic differences among the quartile LAD groups, which did not seem to be a confounding factor in the result.

This study had several limitations. First, this study was limited by its retrospective design. Although the patients who met the inclusion criteria of this study were consecutively en-



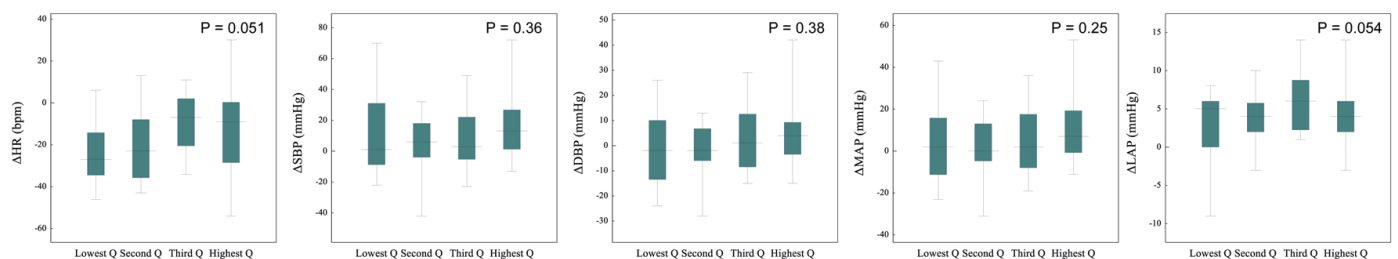
**Table 5.** Comparison of Intraprocedural Parameters Among the Quartile LAD Groups

	Lowest Q (n = 17)	Second Q (n = 19)	Third Q (n = 19)	Highest Q (n = 19)	P value
LAD, mm	37.0 ± 2.9	41.8 ± 0.8	45.2 ± 1.3	51.3 ± 3.1	< 0.001
<b>Pre-measurement</b>					
HR <sub>pre</sub> , bpm	89.9 ± 21.9	89.4 ± 21.5	73.5 ± 13.7	78.1 ± 19.4	0.023
SBP <sub>pre</sub> , mm Hg	97.4 ± 28.2	106.3 ± 21.0	96.9 ± 17.0	102.4 ± 19.3	0.5
DBP <sub>pre</sub> , mm Hg	62.5 ± 14.5	69.2 ± 11.3	60.5 ± 10.6	65.1 ± 14.2	0.19
MAP <sub>pre</sub> , mm Hg	76.9 ± 20.1	84.2 ± 14.2	75.2 ± 12.9	78.4 ± 15.5	0.33
LAP <sub>pre</sub> , mm Hg	7.4 ± 4.6	8.6 ± 3.7	7.8 ± 4.9	7.7 ± 4.6	0.87
<b>Intraprocedural comparison</b>					
Total infusion, mL	1,087.1 ± 428.5	1,125.9 ± 374.2	1,176.8 ± 461.9	1,089.4 ± 440.7	0.91
<b>Sedatives</b>					
Dexmedetomidine, µg	71.5 ± 23.8	72.5 ± 22.3	76.4 ± 27.1	74.7 ± 28.9	0.94
Fentanyl, mg	0.156 ± 0.053	0.176 ± 0.061	0.176 ± 0.051	0.155 ± 0.052	0.45
Diazepam, mg	7.4 ± 3.4	9.0 ± 3.8	7.5 ± 2.8	10.0 ± 3.7	0.067
Thiopental, mg	89.7 ± 42.4	76.3 ± 32.8	97.4 ± 46.3	98.7 ± 43.7	0.33
Contrast agent, mL	28.4 ± 10.1	27.0 ± 11.7	30.1 ± 13.3	26.9 ± 11.6	0.82
Procedure time, min	160.5 ± 43.9	172.0 ± 40.9	165.4 ± 44.4	174.8 ± 57.5	0.8
The time after SR restoration, min	29.0 ± 14.5	25.0 ± 16.6	19.0 ± 13.6	17.0 ± 7.0	0.84
<b>Post-measurement</b>					
HR <sub>post</sub> , bpm	66.0 ± 14.0	68.9 ± 9.4	64.6 ± 8.6	65.3 ± 10.8	0.63
SBP <sub>post</sub> , mm Hg	108.1 ± 23.5	109.7 ± 23.4	105.8 ± 29.7	119.0 ± 26.7	0.43
DBP <sub>post</sub> , mm Hg	61.6 ± 12.1	67.4 ± 13.8	63.3 ± 17.2	70.2 ± 15.9	0.31
MAP <sub>post</sub> , mm Hg	81.1 ± 16.2	83.7 ± 18.8	79.9 ± 22.3	89.6 ± 19.5	0.43
LAP <sub>post</sub> , mm Hg	10.2 ± 3.9	12.2 ± 4.2	13.9 ± 3.6	11.8 ± 3.7	0.044

AF: atrial fibrillation; DBP: diastolic blood pressure; HR: heart rate; LAD: left atrial dimension; LAP: left atrial pressure; MAP: mean arterial pressure; Q: quartile; SBP: systolic blood pressure; SR: sinus rhythm.

rolled between August 2019 and April 2023 in our hospital, there was a selection bias by retrospective design. Second, the subgroups of patients according to AF types, AF-HR quartiles, and LAD quartiles were small; therefore, the statistical power was low, and additional investigations with larger sample sizes are necessary to confirm the results of subgroup analyses. Third, most patients enrolled in the pre-AF group had preserved LVEF (mean ± SD, 59.3 ± 9.6%) and stable heart

failure symptoms (NYHA functional class I, 50%; class II, 50%). Therefore, this study does not provide information on the acute hemodynamic benefits of SR restoration in patients with AF with significantly different characteristics from those enrolled in this study, such as those with depressed LVEF, more severe symptoms (NYHA functional class III/IV), and/or a more rapid ventricular response, and additional investigations are warranted. Forth, thiopental was administered intra-



**Figure 5.** Comparison of the changes in heart rate and blood pressure from before to after pulmonary vein isolation in patients with the quartiles of left atrial dimension. bpm: beats per minute; ΔDBP: change in diastolic blood pressure; ΔHR: change in heart rate; ΔLAP: change in left atrial pressure; ΔMAP: change in mean arterial pressure; Q: quartile; ΔSBP: change in systolic blood pressure.

venously before electrical cardioversion in the pre-AF group but not throughout the procedure in the control group. Although the dose of thiopental used in the pre-AF group was  $1.3 \pm 0.6$  mg/kg, which was considerably less than the usual dose (3 - 4 mg/kg), it could potentially influence the  $MAP_{post}$  and  $LAP_{post}$  in the pre-AF group and become a confounding factor in the results. However, because electrical cardioversion is extremely painful for patients, the use of an additional intravenous anesthetic is unavoidable. In clinical practice, electrical cardioversion is often performed using the same protocol as that used in this study; therefore, we believe that these data can also be applied in clinical settings. Finally, in the pre-AF group, SR restoration was established by internal cardioversion in all patients except for one in whom external cardioversion was performed because of difficulties in placing a 7-Fr electrode catheter in the coronary sinus. In contrast, the control group did not undergo electrical cardioversion because their heart rhythms were SR throughout the procedure. Internal and external cardioversions decrease the left atrial chamber and appendage function [19], which may explain why the LAP was unchanged in the pre-AF group. This problem is difficult to resolve because it is difficult to record a large amount of data on patients with AF who spontaneously return to SR without cardioversion.

## Conclusions

In patients with PAF, atrial contractions may resume quickly, which leads to hemodynamic improvement immediately after cardioversion. As for AF-HR, there was no significant impairment of ventricular diastolic filling at approximately < 109 bpm.

## Acknowledgments

None to declare.

## Financial Disclosure

There was no specific funding source to be mentioned.

## Conflict of Interest

The authors declare that they have no conflict of interest.

## Informed Consent

The requirement for informed consent was waived due to the retrospective nature of the study.

## Author Contributions

TK was involved in the conceptualization, design, supervision,

and analysis of the study and manuscript writing. SM and MO supervised and conducted the analyses, and approved the final manuscript. NM, AI, KT, and NK analyzed and approved the final manuscript.

## Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

## References

1. Rahimtoola SH, Ehsani A, Sinno MZ, Loeb HS, Rosen KM, Gunnar RM. Left atrial transport function in myocardial infarction. Importance of its booster pump function. *Am J Med.* 1975;59(5):686-694. [doi pubmed](#)
2. Linderer T, Chatterjee K, Parmley WW, Sievers RE, Glantz SA, Tyberg JV. Influence of atrial systole on the Frank-Starling relation and the end-diastolic pressure-diameter relation of the left ventricle. *Circulation.* 1983;67(5):1045-1053. [doi pubmed](#)
3. Sanfilippo AJ, Abascal VM, Sheehan M, Oertel LB, Harrigan P, Hughes RA, Weyman AE. Atrial enlargement as a consequence of atrial fibrillation. A prospective echocardiographic study. *Circulation.* 1990;82(3):792-797. [doi pubmed](#)
4. Bonow RO, Frederick TM, Bacharach SL, Green MV, Goose PW, Maron BJ, Rosing DR. Atrial systole and left ventricular filling in hypertrophic cardiomyopathy: effect of verapamil. *Am J Cardiol.* 1983;51(8):1386-1391. [doi pubmed](#)
5. Daoud EG, Weiss R, Bahu M, Knight BP, Bogun F, Goyal R, Harvey M, et al. Effect of an irregular ventricular rhythm on cardiac output. *Am J Cardiol.* 1996;78(12):1433-1436. [doi pubmed](#)
6. Zipes DP. Atrial fibrillation. A tachycardia-induced atrial cardiomyopathy. *Circulation.* 1997;95(3):562-564. [doi pubmed](#)
7. Redfield MM, Kay GN, Jenkins LS, Mianulli M, Jensen DN, Ellenbogen KA. Tachycardia-related cardiomyopathy: a common cause of ventricular dysfunction in patients with atrial fibrillation referred for atrioventricular ablation. *Mayo Clin Proc.* 2000;75(8):790-795. [doi pubmed](#)
8. Rodman T, Pastor BH, Figueroa W. Effect on cardiac output of conversion from atrial fibrillation to normal sinus mechanism. *Am J Med.* 1966;41(2):249-258. [doi pubmed](#)
9. Raymond RJ, Lee AJ, Messineo FC, Manning WJ, Silverman DI. Cardiac performance early after cardioversion from atrial fibrillation. *Am Heart J.* 1998;136(3):435-442. [doi pubmed](#)
10. Roy D, Paillard F, Cassidy D, Bourassa MG, Gutkowska J, Genest J, Cantin M. Atrial natriuretic factor during atrial fibrillation and supraventricular tachycardia. *J Am Coll Cardiol.* 1987;9(3):509-514. [doi pubmed](#)
11. Gertz ZM, Raina A, Saghy L, Zado ES, Callans DJ,

- Marchlinski FE, Keane MG, et al. Evidence of atrial functional mitral regurgitation due to atrial fibrillation: reversal with arrhythmia control. *J Am Coll Cardiol.* 2011;58(14):1474-1481. [doi pubmed](#)
12. Viswanathan K, Daniak SM, Salomone K, Kiely T, Patel U, Converso K, Manning WJ, et al. Effect of cardioversion of atrial fibrillation on improvement in left ventricular performance. *Am J Cardiol.* 2001;88(4):439-441. [doi pubmed](#)
  13. Alam M, Thorstrand C. Left ventricular function in patients with atrial fibrillation before and after cardioversion. *Am J Cardiol.* 1992;69(6):694-696. [doi pubmed](#)
  14. Hsu LF, Jais P, Sanders P, Garrigue S, Hocini M, Sacher F, Takahashi Y, et al. Catheter ablation for atrial fibrillation in congestive heart failure. *N Engl J Med.* 2004;351(23):2373-2383. [doi pubmed](#)
  15. Nogami A, Kurita T, Kusano K, Goya M, Shoda M, Tada H, Naito S, et al. JCS/JHRS 2021 guideline focused update on non-pharmacotherapy of cardiac arrhythmias. *J Arrhythm.* 2022;38(1):1-30. [doi pubmed pmc](#)
  16. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J.* 2016;37(38):2893-2962. [doi pubmed](#)
  17. Manning WJ, Silverman DI, Katz SE, Riley MF, Come PC, Doherty RM, Munson JT, et al. Impaired left atrial mechanical function after cardioversion: relation to the duration of atrial fibrillation. *J Am Coll Cardiol.* 1994;23(7):1535-1540. [doi pubmed](#)
  18. Van Gelder IC, Groenveld HF, Crijns HJ, Tuininga YS, Tijssen JG, Alings AM, Hillege HL, et al. Lenient versus strict rate control in patients with atrial fibrillation. *N Engl J Med.* 2010;362(15):1363-1373. [doi pubmed](#)
  19. Omran H, Jung W, Rabahieh R, Schimpf R, Wolpert C, Hagedorff A, Fehske W, et al. Left atrial chamber and appendage function after internal atrial defibrillation: a prospective and serial transesophageal echocardiographic study. *J Am Coll Cardiol.* 1997;29(1):131-138. [doi pubmed](#)