Increase in pulmonary arterial pressure after atrial fibrillation ablation: incidence and associated findings

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Abstract

Purpose The stiff left atrial (LA) syndrome is defined as pulmonary hypertension (PH) secondary to reduced LA compliance and has recently been shown to be one cause of PH after atrial fibrillation (AF) ablation. We aimed to determine the incidence of an increase in pulmonary arterial (PA) pressure post-ablation and examine the clinical and echocardiographic associations.

Methods Patients who underwent AF ablation between 1999 and 2011 were included if they had both an echocardiogram pre-ablation and 3 months post-ablation. Patients were then separated into two groups with the increased PA pressure group defined as patients with >10 mmHg increase in right ventricular systolic pressure (RVSP) post-ablation and a post-ablation RVSP >35 mmHg.

Results Of the 499 patients meeting the study criteria, 41 (8.2 %) had an increase in RVSP >10 mmHg and RVSP >35 mmHg post-ablation. On echocardiogram, the two groups had similar E/A and E/e' ratios pre-ablation. However, post-ablation, the increased PA pressure group had higher E/A (2.12 vs. 1.49, $p<0.01$) and E/e' (14.7 vs. 11.2, $p<0.01$)

ratios. LA expansion index values were lower in the increased PA pressure group pre-ablation (51 vs. 92 %, $p<0.01$), but not significantly different post-ablation (82 vs. 88 %, $p=0.44$).

Conclusions Around 8 % of patients develop an increase in estimated PA pressure after AF ablation. Echocardiographic parameters suggest that patients who develop increased PA pressure are developing (or unmasking) left ventricular diastolic dysfunction.

Abbreviations

AF	Atrial fibrillation
LA	Left atrial or left atrium
PA	Pulmonary artery
PH	Pulmonary hypertension
RVSP	Right ventricular systolic pressure
TTE	Transthoracic echocardiogram
LV	Left ventricular

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1 Introduction

Pulmonary hypertension (PH), which is most commonly caused by left heart failure, is a significant cause of morbidity and mortality. Pulmonary hypertension from left heart failure is a poor prognostic sign and generally leads to decreased right ventricular (RV) function [1]. One possible cause is a poorly compliant, or stiff, left atrium (LA) causing left atrial diastolic dysfunction. This "stiff left atrial" syndrome was first described in patients after mitral valve surgery [2]. These

patients had right heart failure, dyspnea, and elevated V waves on pulmonary artery wedge pressure measurement.

More recently, it has been shown that this syndrome occurs in patients after radiofrequency catheter ablation for atrial fibrillation (AF). The potential mechanism is thought to be scarring from the ablation itself. A recent study showed that this syndrome caused symptomatic pulmonary hypertension (PH) with elevated V waves in 1.4 % of their patients [3]. While this is certainly a significant portion of patients, it is also possible that there are patients developing PH from ablation that is not immediately symptomatic, but may have long-term adverse effects.

The etiology of this condition is also not fully explained. The scarring of LA myocardium by ablation is a potential cause of decreased compliance and elevated pulmonary pressures. However, the stiff LA syndrome is seen in other conditions such as after mitral valve surgery. In these cases, the mechanism would presumably have to be different.

Complications after catheter ablation for AF such as tamponade and pulmonary vein stenosis are well described [4]. However, the development of PH after ablation, including those patients with the stiff LA syndrome, has not been sufficiently examined. Therefore, we sought to determine the incidence of an increase in pulmonary arterial (PA) pressure post-ablation and identify associated clinical and echocardiographic findings.

2 Methods

This is a retrospective case-control study which was approved by the Mayo Clinic institutional review board. The population included patients who underwent radiofrequency catheter ablation for AF between 1999 and 2011. The procedure consisted of radiofrequency ablation for isolation of all pulmonary veins. Additional linear and focal left and right atrial ablation was performed in patients with persistent atrial fibrillation or inducible arrhythmias after pulmonary vein isolation. For inclusion in this study, patients were required to have the following: (1) a transthoracic echocardiogram (TTE) within 6 months prior to the procedure and (2) a follow-up TTE between 1 week and 6 months after the procedure. These echocardiograms were routinely performed within a few days prior to the procedure and at a 3-month follow-up.

Patients were divided into two groups based on pre- and post-ablation echocardiographic estimation of PA systolic pressures. Pulmonary pressures were estimated using right ventricular systolic pressure (RVSP) on TTE. RVSP was calculated with the formula: $4(V^2)$ + right atrial pressure, where V is the measured peak systolic tricuspid regurgitation velocity and right atrial pressure is estimated based on inferior vena cava diameter and changes with respiration. As there was no evidence of right ventricular outflow tract obstruction, estimated RVSP was assumed equivalent to pulmonary artery systolic pressure.

The case group consisted of patients with increased estimated PA pressure, defined as a >10 mmHg increase in RVSP post-ablation compared to pre-ablation, *and* a post-ablation RVSP>35 mmHg. This was chosen because it was felt that an increase in RVSP of 10 mmHg over a 3-month period is clinically significant; however, we wanted to exclude patients whose post-ablation RVSP was so low as to likely be of no adverse effect.

The majority of the echocardiographic data included in this study was recorded during routine patient care per the current standard practice. Echocardiographic measurements for patients in atrial fibrillation (or other irregular rhythm) are routinely recorded as an average of at least 3 heartbeats. Values that require sinus rhythm, particularly E/A, could not be calculated for patients in atrial fibrillation. Measurement of the LA volume at specific points in the atrial cycle, along with calculation of phasic function based on these measurements, was considered to be potentially useful in explaining the difference between the two groups. However, these values were not included on the routine TTE analysis. Therefore, all echocardiograms from the case group and echocardiograms from a randomly selected 2:1 control group were retrospectively reviewed to measure left atrial volume (by the biplane area-length method) at maximum volume (V_{max}), minimum volume (V_{min}), and prior to atrial systole as denoted by the p wave onset (V_p). To minimize interobserver variability, all measurements were performed by one coauthor. From these volumes, calculations were made to describe the phasic function of the LA. The reservoir phase is described by the LA expansion index=$(V_{max}-V_{min})/V_{min}$; the conduit phase is described by the LA passive emptying fraction=$(V_{max}-V_p)/V_{max}$; and the contractile phase is described by the LA active emptying fraction=$(V_p-V_{min})/V_p$ [5]. The LA expansion index is a simple calculated value that appears to correlate with left atrial stiffness [6].

Demographic and clinical data were obtained during routine care and pulled from the electronic medical record for the study. Valvular disease was defined as moderate or severe regurgitation or stenosis. Assessment for pulmonary vein stenosis was routinely performed on all patients at 3 months by computed tomography scan with contrast or cardiac magnetic resonance imaging. Significant pulmonary vein stenosis was defined as >70 % narrowing of one or more pulmonary veins.

Categorical parameters are presented as percentages of the totals, and any statistical comparisons between groups were completed using a chi-square test for independence. Continuous parameters were summarized using means and standard deviations. The Wilcoxon rank-sum test was used for all comparisons to be consistent. Results were similar between this test and the standard *t* tests. The relationship between individual variables and change in RVSP as a continuous variable was also assessed. Results are reported as a Spearman correlation coefficient.

3 Results

In total, 499 patients met criteria to be included in the study. In the selected time period, there were 2,978 ablations performed for AF including 344 repeat procedures. Of this group, 950 patients had a TTE in both selected time intervals and 499 had an RVSP recorded on both echocardiogram reports.

This group was 72 % male with a mean age of 61 years. Persistent AF ($n=262$, 54 %) was more common than paroxysmal ($n=187$, 39 %), with few patients documented as long-standing persistent atrial fibrillation of greater than 1 year continuous duration ($n=34$, 7 %). For the group as a whole, RVSP increased from 30.8 mmHg pre-ablation to 31.6 mmHg post-ablation ($p=0.02$).

Of the 499 patients, 41 (8.2 %) had an increase of >10 mmHg from pre-ablation to post-ablation RVSP *and* a post-ablation RVSP >35 mmHg. Comparisons of demographic and echocardiographic variables between the two groups are shown in Tables 1 and 2, respectively.

Notably, the group with increased RVSP post-ablation was older (65.1 vs. 60.3 years, $p<0.01$), had a higher body mass index (32.2 vs. 30.1 kg/m^2, $p=0.01$), and was more likely to have coronary artery disease (29.3 vs. 16.8 %, $p=0.05$) and valvular disease (24.4 vs. 10.1 %, $p=0.005$). The type of AF prior to ablation was more likely to be persistent (73.2 vs. 52.5 %, $p=0.01$) rather than paroxysmal (19.5 vs. 40.5 %, $p<0.01$) in the increased RVSP group. Similarly, at the time of the pre-ablation echocardiogram there was a significantly larger percent of patients in atrial fibrillation or atrial flutter (as opposed to sinus rhythm) in the increased RVSP group as compared to the control group (76.9 vs. 38.9 %, $p<0.01$). At the post-ablation echocardiogram, there was a similar percentage of patients in atrial fibrillation or atrial flutter in both groups (5.7 vs. 6.1 %, $p=0.93$). No patients in the group with increased RVSP had evidence of significant pulmonary vein stenosis at 3 months post-ablation.

Comparison of the echocardiographic data reveals that the increased RVSP group had a lower left ventricular ejection fraction pre-ablation (56.2 vs. 59.3 %, $p<0.01$), but this was not significantly different after ablation (59.7 vs. 61.1 %, $p=0.66$). LA volume index pre-ablation was significantly higher in this group (47.3 vs. 39.5 mL/m^2, $p<0.01$), but post-ablation it was not significantly larger (40.2 vs. 39.2 mL/m^2, $p=0.35$).

Mitral valve E/A and E/e' ratios were similar prior to ablation, but after ablation, the increased RVSP group had significantly higher values for both E/A (2.12 vs. 1.49, $p<0.01$) and E/e' (14.70 vs. 11.21, $p<0.01$) ratios. Pulmonary vein systolic to diastolic (S/D) ratios were lower in the increased RVSP group both before (0.71 vs. 1.08, $p<0.01$) and after (0.72 vs. 0.91, $p<0.01$) the procedure.

The comparison of LA phasic function calculations between the two groups is included in Table 3. This revealed a much lower LA ejection fraction in the increased RVSP group (0.30 vs. 0.44, $p<0.01$) prior to ablation, but no difference after ablation (0.42 vs. 0.44, $p=0.44$). This trend was similar for other measurements. The increased RVSP group had a lower pre-ablation LA passive emptying fraction (0.20 vs. 0.25, $p=0.03$), LA active emptying fraction (0.13 vs. 0.25, $p<0.01$), and LA expansion index (0.51 vs. 0.92, $p<0.01$). However, all of these values were similar between groups after ablation.

Table 1 Demographic and clinical characteristics of patients with and without increased right ventricular systolic pressure after atrial fibrillation ablation

	Not increased RVSP ($n=458$)	Increased RVSP ($n=41$)	Total	p
Age (years)	60.3±10.8	65.1±9.0	60.7±10.8	0.01
Male	329 (71.8)	30 (73.2)	359 (71.9)	0.86
BMI (kg/m^2)	30.1±5.7	32.2±5.6	30.3±5.7	0.01
CAD	77 (16.8)	12 (29.3)	89 (17.9)	0.05
Valvular disease	46 (10.1)	10 (24.4)	56 (11.2)	<0.01
Heart failure	40 (8.8)	2 (4.9)	42 (8.4)	0.39
Diabetes mellitus	34 (7.4)	6 (14.6)	40 (8.0)	0.11
Hypertension	228 (49.8)	26 (63.4)	254 (50.9)	0.09
Hyperlipidemia	216 (47.5)	24 (58.5)	240 (48.3)	0.18
Sleep apnea	118 (25.8)	16 (39.0)	134 (26.9)	0.07
Paroxysmal AF	179 (40.5)	8 (19.5)	187 (38.7)	<0.01
Persistent AF	232 (52.5)	30 (73.2)	262 (54.2)	0.01
Permanent AF	31 (7.0)	3 (7.3)	34 (7.0)	0.94

Values are mean±SD or N (%)

AF atrial fibrillation, *BMI* body mass index, *CAD* coronary artery disease, *RFCA* radiofrequency catheter ablation, *RVSP* right ventricular systolic pressure

Table 2 Echocardiographic characteristics of patients with and without increased right ventricular systolic pressure after atrial fibrillation ablation

	Not increased RVSP ($n=458$)	Increased RVSP ($n=41$)	Total	p
LVEF pre-ablation (%)	59.3±9.8	56.2±9.8	59.0±9.8	<0.01
LVEF post-ablation (%)	61.1±8.0	59.7±9.9	61.0±8.2	0.66
Cardiac index pre (L/min/m^2)	3.0±0.7	2.9±0.6	3.0±0.7	0.20
Cardiac index post (L/min/m^2)	3.0±0.6	3.1±0.6	3.0±0.6	0.12
HR pre (bpm)	71.5±19.6	82.9±19.1	72.4±19.8	<0.01
HR post (bpm)	67.1±14.0	68.5±18.3	67.2±14.4	0.86
LA volume index pre (mL/m^2)	39.5±12.8	47.3±14.6	40.1±13.0	<0.01
LA volume index post (mL/m^2)	39.2±11.7	40.2±8.3	39.3±11.4	0.35
RVSP pre (mmHg)	31.1±7.6	27.7±5.1	30.8±7.5	<0.01
RVSP post (mmHg)	30.5±7.2	43.6±8.3	31.6±8.1	<0.01
E/A pre	1.4±0.7	1.3±0.3	1.4±0.6	0.85
E/A post	1.5±0.7	2.1±1.2	1.5±0.7	<0.01
E/E' pre	10.4±4.5	9.9±2.9	10.3±4.4	0.82
E/E' post	11.2±5.2	14.7±8.4	11.5±5.6	<0.01
S/D pre	1.1±0.5	0.7±0.3	1.1±0.5	<0.01
S/D post	0.9±0.4	0.7±0.4	0.9±0.4	<0.01

Values are mean±SD

AF atrial fibrillation; *E/A* mitral E/A, *E/E'* mitral E/medial E', *HR* heart rate, *LA* left atrial, *LVEF* left ventricular ejection fraction, *RVSP* right ventricular systolic pressure, *S/D* pulmonary vein S/D

The change in RVSP from pre-ablation to post-ablation as a continuous variable was compared to demographic and echocardiographic parameters. The pre-ablation mitral valve E/A and E/e' ratios did not have a statistically significant correlation with change in RVSP. However, post-ablation E/A ($r=0.26$, $p<0.01$) and E/e' ($r=0.11$, $p=0.02$) ratios showed a correlation with change in RVSP. LA volume showed the opposite trend with a slight correlation pre-ablation ($r=0.16$, $p<0.01$), but no correlation post-ablation. Pulmonary vein S/D showed a slight correlation pre-ablation ($r=-0.12$, $p=0.03$) and post-ablation ($r=-0.24$, $p<0.01$).

4 Discussion

The key findings from this study are the following: (1) 8.2 % of our patients had an increase in estimated pulmonary pressure after undergoing ablation for atrial fibrillation and (2)

Table 3 Left atrial phasic function measurements in patients with and without increased right ventricular systolic pressure after atrial fibrillation ablation

	Not increased RVSP ($n=90$)	Increased RVSP ($n=37$)	p
LA EF pre-ablation	0.44±0.14	0.30±0.16	<0.01
LA EF post-ablation	0.44±0.13	0.42±0.13	0.44
LA minimum volume pre	43.0±22.9	58.1±25.3	<0.01
LA minimum volume post	40.7±22.4	47.5±18.9	0.02
LA passive emptying fraction pre	0.25±0.13	0.20±0.10	0.03
LA passive emptying fraction post	0.23±0.10	0.25±0.11	0.58
LA active emptying fraction pre	0.25±0.17	0.13±0.15	<0.01
LA active emptying fraction post	0.27±0.15	0.23±0.13	0.13
LA expansion index pre	0.92±0.52	0.51±0.37	<0.01
LA expansion index post	0.88±0.50	0.82±0.44	0.44

Values are mean±SD

AF atrial fibrillation, *EF* ejection fraction, *LA* left atrial, *RVSP* right ventricular systolic pressure

analysis of echocardiographic findings suggests that the development or "unmasking" of left ventricular (LV) diastolic dysfunction is commonly associated.

Comparison of the two groups revealed that the group with an increase in RVSP had many echocardiographic findings consistent with LV diastolic dysfunction. Mean E/A in the increased RVSP group was in the normal range prior to ablation, but increased to >2 after ablation. An E/A ratio in this range is commonly seen in patients with advanced LV diastolic dysfunction. The E/E' also increased dramatically in the group with increased RVSP, suggesting increased LV filling pressure consistent with LV diastolic dysfunction. Similar findings were seen when comparing these parameters to the change in RVSP as a continuous variable; however, the correlation coefficients were low. These differences were generally not present before ablation, but were significant after ablation, suggesting that these patients develop LV diastolic dysfunction after ablation. This could potentially happen from an effect of the ablation itself, from a change in rhythm, from a long-term effect of change in volume status, or natural progression of the disease. Ablation could *cause* LV diastolic dysfunction by inducing constrictive pericarditis due to pericardial inflammation or by inducing ischemia with injury of a coronary artery.

An alternative hypothesis is that this may represent an "unmasking" of LV diastolic dysfunction. In other words, the diastolic dysfunction is present before the procedure but not seen in the typical echocardiographic parameters due to limitations of echocardiography, volume status, or other causes. In accordance with this hypothesis, not all findings suggestive of LV diastolic dysfunction were absent prior to ablation. The group with increased RVSP had large left atria prior to ablation that were significantly larger than the unaffected group. The LA volume index typically increases with worsening LV diastolic dysfunction, so this supports the possibility that LV diastolic dysfunction may have already been present. Furthermore, patients in the increased RVSP group were more likely to have other risk factors for LV diastolic dysfunction, such as increased age, obesity, and coronary artery disease.

One way in which ablation might lead to this unmasking is with a decrease in the size of the LA, as was seen in the increased RVSP group. Pre-ablation, the enlarged LA may act as a capacitance chamber, accepting the extra volume to be delivered to the LV and preventing an increase in the pulmonary pressure over time. When the LA size is reduced after ablation, the extra blood volume must be accommodated by the pulmonary vasculature causing an increase in pulmonary pressures. The LA may still be able to accept the same ratio of volume per change in pressure and thus have the same compliance. Therefore, it could be the lack of volume in the LA that leads to elevated pulmonary pressure without any increase in LA stiffness. Further validation would be needed in animal or human studies.

Overall, the findings suggest that LV diastolic dysfunction is more commonly associated with pulmonary hypertension after ablation than LA diastolic dysfunction. Also, while not a direct measure of atrial compliance, the LA expansion index was similar between these two groups after ablation. This suggests that the increased PA pressures are not from a poorly compliant or "stiff" LA. Despite these findings, this study does not eliminate stiff LA syndrome as a possible cause of PH in some patients. Some of the echocardiographic findings suggestive of LV diastolic dysfunction could also correlate with LA diastolic dysfunction. In addition, with stiff LA syndrome only seen in 1.4 % of patients in a previous study [3], it is possible that a similar number in our group had a stiff LA, but data from this subgroup was diluted by patients developing increased RVSP from LV diastolic dysfunction or other reasons.

4.1 Limitations

The limitations of this study are similar to those of other retrospective studies. Ideally, all patients would undergo catheterization with direct measurement of cardiac pressures and compliance. However, cardiac catheterization was not routinely performed in the normal clinical course of these patients and is therefore unavailable in this retrospective study. Echocardiographic measurements were used to estimate intracardiac pressures as well as systolic and diastolic function. Some of the parameters of LA expansion and compliance do not have rigorous animal or human studies for validation of correlation with invasive measurements. While many of the echocardiography findings are quite suggestive of LV diastolic dysfunction, the echocardiographic parameters that would be seen with an isolated reduction in LA compliance are not fully defined and may overlap with those of LV diastolic dysfunction.

We were primarily aiming to define the incidence of this disease and examine the echocardiographic and clinical associations, so specific ablation techniques were not examined, but may have had an impact on outcomes. The primary reason patients were excluded from the study was due to lack of an echocardiogram during the appropriate time period or lack of a recorded RVSP. This was generally thought to be due to random lack of data but could have possibly introduced a bias. Given the retrospective nature of the study, cause and effect relationships cannot be evaluated. Therefore, our conclusions can only be hypothesis generating.

5 Conclusions

This study shows that increased pulmonary artery pressure is common after atrial fibrillation ablation. Echocardiographic findings suggest that the most common association appears to

be the development or unmasking of left *ventricular* diastolic dysfunction.

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