

## ORIGINAL ARTICLE

# Impact of impedance decrease during radiofrequency current application for atrial fibrillation ablation on myocardial lesion and gap formation

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**Abstract**

**Background:** The clinical impact of a decrease in impedance during radiofrequency catheter ablation (RFCA) has not been fully clarified. The aim of the study was to analyze the impact of impedance decrease and to determine its optimal cutoff value during RFCA.

**Methods:** We evaluated 34 consecutive patients (total 3264 lesions, mean age  $66 \pm 8.7$  years, 10 females) who underwent their first ablation for atrial fibrillation (AF). The impedance decrease, average contact force (CF), application time, force-time integral (FTI), product of impedance decrease and application time (PIT), and the product of impedance decrease and FTI (PIFT) were measured for all lesions. Levels of cardiac troponin I (TrpI) were measured for assessment of myocardial injury. The incidence of intraprocedural pulmonary vein-left atrium reconnection or dormant conduction (reconnection) was determined. The relationships between the ablation parameters and the increase in TrpI ( $\Delta$ TrpI) were evaluated. The predictive value of the parameters for reconnection was assessed using receiver operating characteristic (ROC) curve analysis.

**Results:** Reconnection was detected in 18 patients. Average FTI and PIT were significantly correlated with  $\Delta$ TrpI (FTI:  $r^2 = .19$ ,  $P = .0090$ , PIT:  $r^2 = .21$ ,  $P = .0058$ ). PIFT was correlated with  $\Delta$ TrpI and was the best of the three indexes (PIFT:  $r^2 = .29$ ,  $P = .0010$ ). In ROC curve analysis, the area under the curve for predicting reconnection was 0.71 and the optimal cutoff value was 5200 for PIFT (sensitivity 78%, specificity 63%).

**Conclusion:** The combination of CF and a decrease in impedance could be important in the evaluation of myocardial lesions and reconnection during RFCA.

**KEYWORDS**

atrial fibrillation, contact force, gap formation, impedance decrease, radio-frequency catheter ablation, troponin I

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## 1 | INTRODUCTION

Radiofrequency catheter ablation (RFCA) has made major advances and the long-term efficacy of pulmonary vein isolation (PVI) for drug-refractory paroxysmal atrial fibrillation (PAF) has been widely reported.<sup>1,2</sup> During PVI by RFCA, the formation of a gap in the ablation line could cause recurrence of AF and atrial tachycardia.<sup>3,4</sup> Some parameters during ablation have been reported as useful for avoiding gap formation. Several experimental studies have shown that catheter-tissue contact force (CF) is an important determinant of the lesion size during radiofrequency application.<sup>5–7</sup> Recently, a CF sensing catheter has been available and monitoring of real-time CF during radiofrequency application has become possible. Previous reports have described the clinical outcomes of CF-guided ablation, which had been considered to be effective and safe for PAF.<sup>8–10</sup> However, although CF is an important index, it does not completely express the amount of energy transferred between the electrode and the ablated tissue, which determines the myocardial temperature. Myocardial injury would be dependent on the temperature of tissue heated by radiofrequency current,<sup>11</sup> but direct measurement of the tissue temperature or the damage to the myocardium is impossible. Other surrogate parameters, such as initial impedance, amplitude, impedance drop during ablation, and electrode temperature, have been reported previously as criteria of the ablation effect,<sup>12–14</sup> but the initial impedance and amplitude of the local electrocardiogram were reported by some previous studies to be less effective indexes in relation to CF.<sup>15,16</sup> Impedance drop during radiofrequency delivery is also a marker of tissue heating. In heated tissue by radiofrequency, movement of ions can be promoted and it provides high ion conductivity, resulting in a drop in impedance to current flow. There have been previous reports that a drop in impedance could be correlated with CF<sup>17,18</sup> and predictive of the ablation effect or clinical outcome,<sup>16,19,20</sup> but the impact of an impedance drop remains to be fully elucidated. The aim of this study was to clarify whether a decrease in impedance could predict myocardial injury from the application of RFCA in the human beating heart and whether it could predict the acute outcome of PVI.

## 2 | METHODS

Thirty-four consecutive patients (mean age  $66 \pm 8.7$  years, 24 males, 22 patients with PAF, 3292 ablation lesions) who underwent a first AF ablation in Musashino Red Cross Hospital were included. Clinical characteristics were recorded and the impedance drop, average CF, and application time were determined at each ablation site. Impedance was measured between the catheter tip and the earth patch positioned on the patient's left side using 60 kHz current. If the impedance changed dramatically when the ablation catheter moved (total 62 sites), or impedance increased during RFCA (35 sites), radiofrequency application was stopped and we assessed the stable impedance value manually before any impedance change for the measurement of impedance drop (Figure 1). We also excluded

28 ablation sites where the application was stopped within 5 second for any reason; the remaining 3264 lesions were analyzed. Impedance during RFCA was recorded by an investigator blinded to the CF. All patients provided written informed consent and the ethics committee of Musashino Red Cross Hospital approved this study.

### 2.1 | Myocardial lesion and ablation parameters

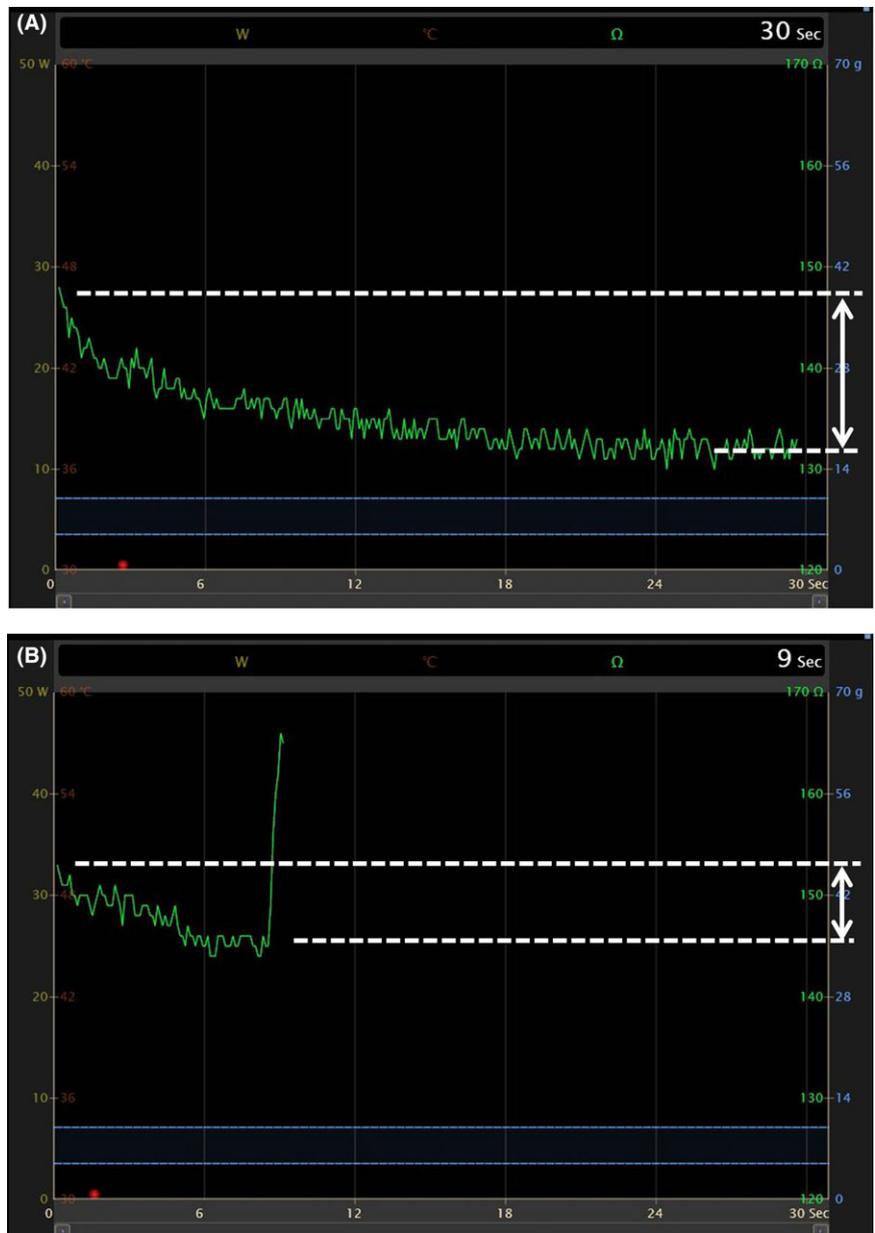
This study consisted of two parts. One assessed the relationship between impedance drop and ablation effect. For the assessment of myocardial injury by radiofrequency current, we selected cardiac troponin I (TrpI) as a marker of myocardial lesions, which is usually used in the diagnosis of acute coronary syndrome. The impedance drop, average CF, and the application time of the initial 50 applications in each patient (total 1700 lesions), as well as TrpI levels before ablation and after the 50th application, were determined prospectively. As parameters for analysis, we used the force-time integral (FTI; defined as the product of CF and application time), the product of impedance drop and application time (PIT), and the product of impedance drop and FTI (PIFT). The relations between the mean values of FTI, PIT, and PIFT for the initial 50 radiofrequency applications and the increase in TrpI after 50 applications ( $\Delta$ TrpI) were studied.

### 2.2 | Predictive value of the parameters for acute ablation outcome

The second part of this study was concerned with the acute clinical outcomes. Intra-session left atrium-pulmonary vein reconnection and/or dormant conduction was defined as reconnection during the PVI session.<sup>21</sup> Patients were divided into those with no reconnection during the session (nonreconnection group;  $n = 16$ , total 1441 lesions) and the reconnection group ( $n = 18$ , total 1823 lesions). Differences in clinical characteristics and ablation parameters were compared between the two groups. Optimal cutoff values of PIT and PIFT were determined using receiver operating characteristic (ROC) curve analysis.

### 2.3 | Method of PVI

Any antiarrhythmic drugs were discontinued 1 week before RFCA. All patients had effective anticoagulation before the sessions. If warfarin was taken, it was continued on the day of the procedure, while if a direct oral anticoagulant was prescribed, it was skipped only on the morning of the session. A duodecapolar catheter was inserted via the right subclavian vein to the coronary sinus, and a quadripolar or decapolar catheter was advanced to the right ventricle via the right femoral vein. After a transeptal puncture, TrpI at preablation was sampled and two decapolar ring catheters were inserted to the pulmonary veins. An activated clotting time of over 300 second was maintained with a continuous infusion of heparin during the session. PVI was performed by 5 operators using the point-by-point method, with assistance from a three-dimensional electroanatomical mapping system (CARTO3; Biosense Webster). All ablation parameters,



**FIGURE 1** Impedance curve during radiofrequency current application. The change in impedance during radiofrequency current application is shown in the upper panel. (A) Impedance decrease was measured as shown by the arrow. If the impedance changed dramatically, (B) the application was stopped. The stable value of impedance before the impedance change was then measured manually and the impedance decrease was calculated (lower panel)

including CF and impedance, were freely available to the operators during RFCA, and all applications were open-ended and not limited by any parameters such as FTI or impedance, only being stopped in response to a rise in impedance. All ablated points were anatomically decided and were ablated 25 to 30 seconds. If bipolar electrocardiogram of distal tip of ablation catheter would be complete QS form, radiofrequency delivery was stopped at least 20 seconds after the beginning of ablation by the operator's decision. All patients received intravenous anesthesia by continuous infusion of dexmedetomidine with a pentamidine bolus. Radiofrequency current applications were delivered via a 3.5 mm tipped open-irrigated catheter (Smart Touch; Biosense Webster) with a target temperature of 43°C. The maximum power settings were 25 W on the posterior wall and 30 W on the anterior wall of the pulmonary veins. Esophageal temperature was measured during the application. After the 50th application, TrpI was measured from a blood sample collected from the sheath of the

catheter located in the right atrium. After PVI was completed, collection of the data for CF, impedance drop, and application time was completed, and a waiting time of 15 minutes was set, including the time for cavotricuspid isthmus ablation. If intra-session left atrium-pulmonary vein reconnection was not detected in this period, even after 1 gamma of isoproterenol infusion, rapid intravenous injection of adenosine triphosphate (ATP), 0.4 mg/kg body weight, was performed to unmask dormant conduction. When dormant conduction was provoked by the ATP infusion, additional radiofrequency current applications were performed until dormant conduction was disappeared.

## 2.4 | Statistical analysis

Continuous variables are given as mean  $\pm$  standard deviation if normally distributed or as median with interquartile range otherwise.

Categorical variables are given as count and percentage. Continuous data were compared using Student's t-test when normally distributed or the Mann-Whitney *U* test when not. Categorical data were compared by  $\chi^2$  test across the groups. Single regression analysis was performed to study the relation between FTI, PIT and PIFT, and  $\Delta$ Trpl. Clinical manifestations and ablation parameters for patients with and without intra-session reconnection were analyzed using univariable analysis. Multivariable analysis was not performed because most of the variables that showed a significant difference between the two groups in univariable analysis were strongly correlated with the impedance decrease. ROC curve analysis was performed to determine the optimal cutoff value of PIFT that gave the best sensitivity and specificity. All tests were two-sided, and a value of  $P < .05$  was considered statistically significant. Analyses were performed with JMP® 8.0.1 software (SAS Institute Inc., Cary, NC).

### 3 | RESULTS

#### 3.1 | Myocardial injury and ablation parameters

The baseline characteristics of the study population are shown in Table 1. Approximately two-thirds of the patients had PAF and the mean left atrial diameter was 37 mm. The average CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>Vasc scores of this population were not high and most patients had a preserved left ventricular ejection fraction. Table 2 shows the ablation parameters for the initial 50 lesions in each patient. The initial impedance was 148  $\Omega$  and all lesions were ablated 20 W and over. The average contact force was 18  $\pm$  4.1 g and the impedance drop was 9.0  $\pm$  1.8  $\Omega$ . The average initial impedance of these 50 ablation sites was not significantly correlated with  $\Delta$ Trpl ( $\Delta$ Trpl =  $-0.81 + 0.80 \times$  FTI,  $r^2 = .046$ ,  $P = .23$ ). The average impedance decrease tended to be correlated with the average of FTI, but the association did not reach statistical significance (FTI =  $290 + 23 \times$  impedance decrease,  $r^2 = .098$ ,  $P = .077$ ).  $\Delta$ Trpl was significantly correlated with both FTI and PIT, but the correlations were relatively weak. ( $\Delta$ Trpl =  $23 + 0.18 \times$  FTI,  $r^2 = .19$ ,  $P = .0090$ ;  $\Delta$ Trpl =  $-0.076 + 0.45 \times$  PIT,  $r^2 = .21$ ,  $P = .0058$ ; Figure 2) The

**TABLE 1** Baseline characteristics of the 34 patients

n = 34	
Age (years)	66 $\pm$ 8.7
Male gender (%)	24 (71%)
PAF (%)	22 (65%)
CHADS <sub>2</sub>	0 [0-1.25]
CHA <sub>2</sub> DS <sub>2</sub> Vasc	1.5 [0-3]
SSS (%)	6 (18%)
LAD (mm)	37 $\pm$ 7.2
LVEF (%)	67 $\pm$ 7.9
BNP (pg/mL)	62 [10-320]
eGFR (mL/min/1.73 m <sup>2</sup> )	72 $\pm$ 17

BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; LAD, left atrial diameter; LVEF, left ventricular ejection fraction; PAF, paroxysmal atrial fibrillation; SSS, sick sinus syndrome.

**TABLE 2** Mean values of ablation parameters from the initial 50 applications and levels of cardiac troponin I before and after 50 applications

n = 34 (1700 lesions)	
Impedance, initial ( $\Omega$ )	148 $\pm$ 14
Power (W)	27 $\pm$ 1.3
Application time (s)	27 $\pm$ 2.4
Average CF (g)	18 $\pm$ 4.1
Impedance decrease ( $\Omega$ )	9.0 $\pm$ 1.8
Trpl, initial (pg/mL)	17.6 $\pm$ 11.8
Trpl, after 50th application (pg/mL)	128 $\pm$ 60.2

CF, contact force; Trpl, cardiac troponin I.

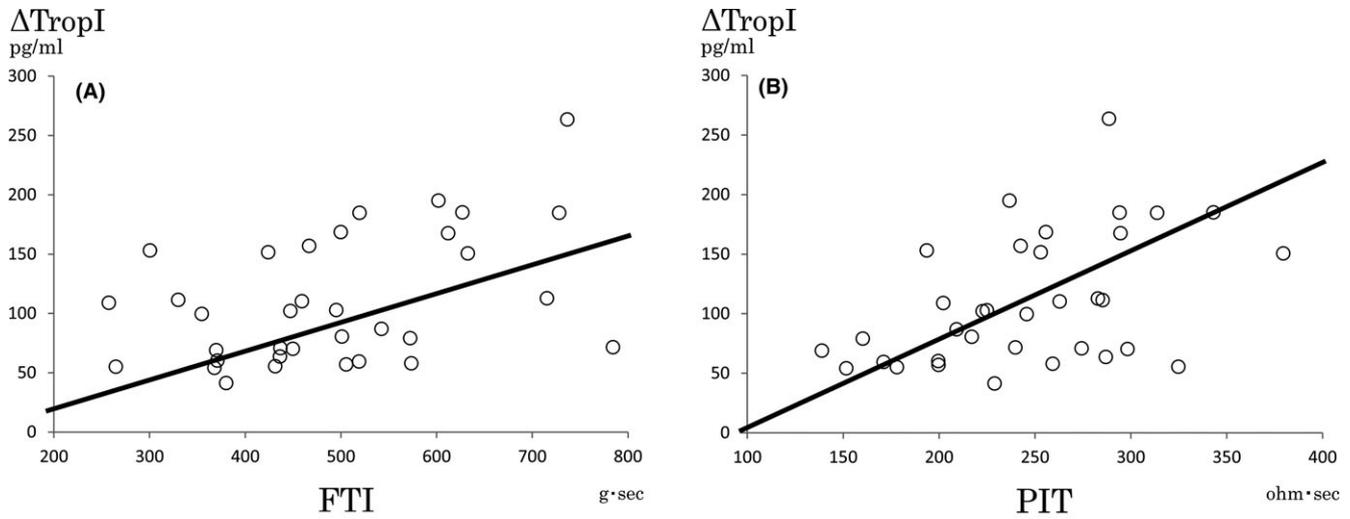
combined index, PIFT, was the best correlated of all the three indexes ( $\Delta$ Trpl =  $34 + 0.016 \times$  PIFT,  $r^2 = 0.29$ ,  $P = .0010$ ; Figure 3)

#### 3.2 | Predictive value for acute outcome

The baseline characteristics, clinical data, and ablation parameters of the two groups are shown in Table 3. Age, gender, AF type, embolism risk score, presence of sick sinus syndrome, brain natriuretic peptide levels, and estimated glomerular filtration rate did not differ significantly between the two groups. Left atrial diameter was significantly larger in the group with reconnection during the session. (nonreconnection 34  $\pm$  5.9 mm, reconnection 39  $\pm$  7.6 mm,  $P = .049$ ) Initial impedance (nonreconnection 150  $\pm$  16  $\Omega$ , reconnection 140  $\pm$  14  $\Omega$ ,  $P = .14$ ) and average CF (nonreconnection 20  $\pm$  3.5 g, reconnection 18  $\pm$  3.2 g,  $P = .12$ ) tended to be higher in the nonreconnection group, but the difference did not reach statistical significance. The impedance drop was significantly higher in the nonreconnection group than in the reconnection group (nonreconnection 10  $\pm$  1.7  $\Omega$ , reconnection 8.6  $\pm$  1.3  $\Omega$ ,  $P = .012$ ). There was no significant difference between the two groups in FTI (nonreconnection 520  $\pm$  100 g.s, reconnection 480  $\pm$  96 g.s,  $P = .29$ ). Both PIT and PIFT were significantly higher in the nonreconnection group than in the reconnection group (PIT: nonreconnection 270  $\pm$  46  $\Omega$ .s, reconnection 240  $\pm$  39  $\Omega$ .s,  $P = .029$ ; PIFT: nonreconnection 5600  $\pm$  340 g. $\Omega$ .s, reconnection 4500  $\pm$  320 g. $\Omega$ .s,  $P = .024$ ). ROC curve analysis revealed that the area under the curve for predicting reconnection during the session was 0.69 for PIT, and 0.71 for PIFT. The optimal cutoff value for predicting reconnection during the session was 280  $\Omega$ .s for PIT (sensitivity 89%, specificity 50%) and 5200 g. $\Omega$ .s for PIFT (sensitivity 78%, specificity 63%; Figure 4).

### 4 | DISCUSSION

This study assessed the relationship between ablation parameters and Trpl, and assessed the impact of an impedance decrease on the acute outcome of AF ablation. This is the first report to demonstrate that an impedance decrease during radiofrequency application could reflect myocardial injury in human beating hearts, assessed indirectly using Trpl sampling. Trpl is a subunit of the troponin complex, and elevation of serum levels of Trpl is considered to reflect myocardial injury.<sup>22</sup> Some



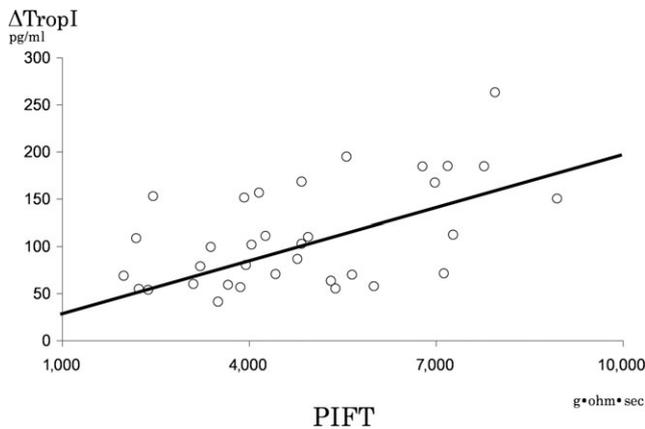
**FIGURE 2** Relationships between FTI, PIT, and ΔTrpI. The relationships of FTI and PIT to ΔTrpI are shown in Figure 2. There were significant correlations between FTI and ΔTrpI (A), and between PIT and ΔTrpI (B) ( $\Delta\text{TrpI} = 23 + 0.18 \times \text{FTI}$ ,  $r^2 = .19$ ,  $P = .0090$ ;  $\Delta\text{TrpI} = -0.076 + 0.45 \times \text{PIT}$ ,  $r^2 = .21$ ,  $P = .0058$ ). However, the correlation coefficients were not very high. FTI, force-time integral; PIT, product of impedance decrease during the application and application time, ΔTrpI, increase in cardiac troponin I after 50 radiofrequency applications

previous studies showed that cardiac biomarkers, including TrpI, were elevated after catheter ablation as a result of myocardial injury caused by the radiofrequency current.<sup>23,24</sup> The results of the present study indicate that both CF and a drop in impedance were correlated with myocardial injury. Furthermore, a new index, PIFT, combining both CF and impedance drop, had the strongest correlation, although the correlation coefficient was not very high ( $r^2 = .29$ ). This may be because TrpI elevation is not only dependent on myocardial injury by radiofrequency current, but can also be attributable to other factors, including inflammation of the surrounding myocardium, the volume and density of the surrounding myocardium, edema, minute ischemia induced by ablation, and the sampling variability of TrpI.

The other new finding of this study was the optimal cutoff value for impedance decrease as a predictor of the acute outcome. Based on our results, the optimal cutoff values that gave the highest

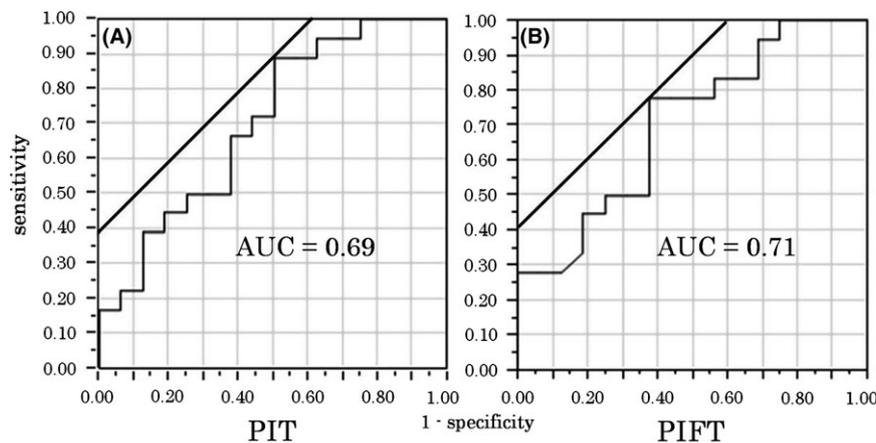
**TABLE 3** Differences in baseline characteristics, ablation parameters, and indexes derived from ablation parameters in the two groups

	No reconnection during the session n = 16 (1441 lesions)	Reconnection during the session n = 18 (1823 lesions)	P value
Age (y)	65 ± 8.7	67 ± 8.8	.49
Male gender (%)	9 (56%)	15 (83%)	.13
PAF (%)	10 (63%)	12 (67%)	.8
CHADS <sub>2</sub>	0 [0-1]	1 [0-2]	.16
CHA <sub>2</sub> DS <sub>2</sub> Vasc	2 [0.25-3]	1 [0-4]	.87
SSS (%)	2 (13%)	4 (22%)	.46
LAD (mm)	34 ± 5.9	39 ± 7.6	.049
LVEF (%)	66 ± 8.5	68 ± 7.4	.34
BNP (pg/mL)	59 [27-130]	97 [51-210]	.48
eGFR (mL/min/1.73 m <sup>2</sup> )	74 ± 17	71 ± 19	.57
Impedance, initial (Ω)	150 ± 16	140 ± 13	.14
Power (W)	27 ± 0.91	28 ± 1.3	.38
Application time (s)	27 ± 1.5	27 ± 1.8	.33
Average CF (g)	20 ± 3.5	18 ± 3.2	.12
Impedance decrease (Ω)	10 ± 1.7	8.6 ± 1.3	.012
TrpI, initial (pg/mL)	18 ± 11	18 ± 12	.97
TrpI, after 50th application (pg/mL)	400 ± 93	440 ± 82	.73
FTI (g.s)	520 ± 100	480 ± 96	.29
PIT (Ω.s)	270 ± 46	240 ± 39	.029
PIFT (g.Ω.s)	5600 ± 340	4500 ± 320	.024



**FIGURE 3** Relationship between PIFT and ΔTrpI. PIFT had a significantly better correlation with ΔTrpI than did FTI or PIT ( $\Delta\text{TrpI} = 34 + 0.016 \times \text{PIFT}$ ,  $r^2 = .29$ ,  $P = .0010$ ). PIFT, product of impedance decrease and FTI. Other abbreviations as in Figure 2

FTI, Force-time integral; PIFT, product of impedance decrease and FTI; PIT, product of impedance decrease and application time. Other abbreviations as in Tables 1 and 2.



**FIGURE 4** Receiver operating characteristic curve analyses for PIT and PIFT. Receiver operating characteristic curve analyses for PIT and PIFT are shown in Figure 4. The analyses revealed that the area under the curve for predicting reconnection during the session was 0.69 for PIT and 0.71 for PIFT, with the optimal cutoff values for predicting reconnection being 280  $\Omega$ .s for PIT (sensitivity 89%, specificity 50%) (A) and 5200 g. $\Omega$ .s for PIFT (sensitivity 78%, specificity 63%) (B). Abbreviations as in Figure 3

predictive value were 5200 g. $\Omega$ .s for PIFT and 280  $\Omega$ .s for PIT. Previous studies reported that FTI should be maintained at over 400–500 g.s.<sup>25–28</sup> Taking these results together, if FTI is maintained at 500 g.s, the recommended impedance drop would be over 11  $\Omega$ . It is important to note that, in the present study, the average FTI in each group was maintained at a sufficient level in accordance with previous reports,<sup>25–28</sup> because the operators were not blinded to the CF during RFCA. Therefore, our results indicate that the impedance decrease could be more important, especially in RFCA sessions when an adequate CF is maintained.

There have been reports that CF and impedance drop showed a good correlation in ex vivo experiments<sup>17,18</sup> and in vivo analysis.<sup>28</sup> However, although the present study found a trend towards a correlation between the two parameters, the association was not statistically significant. One likely reason for this result might be that the assessment was performed in human beating hearts under spontaneous respiration. Second, this study assessed only the average values of the ablation parameters, without evaluating any differences in CF between individual ablation sites. Ullah et al reported that a higher CF induced a greater impedance drop.<sup>24</sup> A more comprehensive analysis, including all the ranges of CF, might lead to different results. Third, the analysis was performed without taking account of the location of the ablation site or the catheter orientation, whereas a previous report showed that the impedance decrease during RFCA is influenced by these two factors.<sup>19</sup>

Our data did not indicate that the impedance decrease was more important than the CF. CF was maintained at the majority of ablation points in this study and all analyses were performed under this assumption. But there were variation of impedance drop in some ablated points despite similar CF and application time. Possible reason of this result would be that wall thickness and tissue dense of the ablated points or catheter stability could affect impedance drop. This might suggest that impedance decrease during ablation could reflect tissue factor as well. Concerning these aspects, operators might consider to ablate longer time, to stabilize catheter, and to ablate with higher power setting when sufficient impedance drop would not be achieved with significant CF.

Thus, our findings suggest that monitoring of impedance during ablation should be recommended for the estimation of lesion size and for avoiding gap formation. A prospective analysis will be needed to evaluate the impact of impedance- and PIFT-targeted PVI.

#### 4.1 | Study limitations

This study had some limitations. First, it did not include data relating to catheter location and orientation, which might have affected the impedance values. Second, the impact of an impedance rise during RFCA could not be assessed because in this study the RF application was stopped when impedance increased. Third, dormant conduction and intra-procedure reconnection between the pulmonary veins and left atrium were defined as endpoints in the present study. However, the waiting period was only 15 min after the completion of the first PVI, while the clinical impact of dormant conduction remains controversial.<sup>21,29</sup> It would be difficult to estimate long-term outcomes from our results.

## 5 | CONCLUSIONS

CF and impedance decrease during ablation were correlated with myocardial injury, and the combined index that included both CF and impedance decrease had a higher significant correlation with myocardial injury, as assessed by TrpI than either of the single indexes. In addition, PIT and PIFT were able to predict intra-session left atrium-pulmonary vein reconnection and dormant conduction under the condition of preserved CF. Further prospective analysis will be necessary to clarify the impact of impedance drop and the combined index as targets during PVI.

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**CONFLICT OF INTEREST**

Authors declare no conflict of interests for this article.

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