Relationship between device-detected subclinical atrial fibrillation and heart failure in patients with cardiac resynchronization therapy defibrillator

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Abstract

Background: Atrial fibrillation (AF) is a leading preventable cause of heart failure (HF) for which early detection and treatment is critical. Subclinical-AF is likely to go untreated in the routine care of patients with cardiac resynchronization therapy defibrillator (CRT-D).

Hypothesis: The hypothesis of our study is that subclinical-AF is associated with HF hospitalization and increasing an inappropriate therapy.

Methods: We investigated 153 patients with an ejection fraction less than 35%. We divided into three groups, subclinical-AF (n = 30), clinical-AF (n = 45) and no-AF (n = 78). We compared the baseline characteristics, HF hospitalization, and device therapy among three groups. The follow-up period was 50 months after classification of the groups.

Results: The average age was 66 ± 15 years and the average ejection fraction was 26 ± 8%. Inappropriate therapy and biventricular pacing were significantly different between subclinical-AF and other groups (inappropriate therapy: subclinical-AF 13% vs clinical-AF 8.9% vs no-AF 7.7%, P = .04, biventricular pacing: subclinical-AF 81% vs clinical-AF 85% vs no-AF 94%, P = .001). Using Kaplan-Meier method, subclinical-AF group had a significantly higher HF hospitalization rate as compared with other groups. (subclinical-AF 70% vs clinical-AF 49% vs no-AF 38%, log-rank: P = .03). In multivariable analysis, subclinical-AF was a predictor of HF hospitalization.

Conclusions: Subclinical-AF after CRT-D implantation was associated with a significantly increased risk of HF hospitalization. The loss of the biventricular pacing and increasing an inappropriate therapy might affect the risk of HF hospitalization.

KEYWORDS
cardiac resynchronization therapy, heart failure, inappropriate therapy, subclinical atrial fibrillation
Cardiac resynchronization therapy with defibrillator (CRT-D) is an approved treatment for patients with an advanced staged of heart failure (HF) in sinus rhythm (SR) with low left ventricular ejection fraction (LVEF) and ventricular dyssynchrony. This therapy is associated with a reduction in symptoms, improvement in LVEF, and decrease in hospitalization and mortality. However, the appropriate use of CRT is not well defined in patients with atrial fibrillation (AF). CRT is not as effective in patients with AF because of inadequate biventricular capture and loss of atrioventricular (AV) synchrony. A recent study showed that ablation of the AV junction ablation was associated with a significantly reduced likelihood and rate of AF-related hospitalization, irrespective of whether a right ventricular (RV) or a biventricular pacemaker was implanted. In patients who underwent ablation of the AV junction, implantation of a biventricular pacemaker was associated with a 38% reduction in the rate of HF hospitalizations as compared with patients who had an RV pacemaker. AF might be symptomatic and asymptomatic, or both. Therefore, HF or stroke can be the first clinical manifestation of asymptomatic AF. The Assert study showed that subclinical-AF (S-AF) was associated with stoke event. However, these studies found no relationship between S-AF and HF hospitalization. Furthermore, the relationship between S-AF and HF hospitalization is still unclear, and S-AF is likely to go untreated in patients with CRT-D. The purpose of this study was to investigate the relationship between S-AF and HF hospitalization in patients with cardiac dysfunction using CRT-D.

We evaluated the patients’ baseline clinical characteristics using data obtained from the electronic medical records, the telephone contact for the patient’s family, and the device report. We also examined the records to determine HF hospitalization, stroke, and cardiac event. In addition, we evaluated implantable cardioverter defibrillator (ICD) therapies from the device reports, including shock therapy and anti-tachycardia pacing (ATP) therapy. ATP was attempted with eight pulses at 88% of the measured cycle length with a 10-ms decrement between bursts. The initial device shock was attempted at the attending physician’s discretion. The remaining device shock consisted of the maximal energy shocks. The ICD was programmed at the attending physician's discretion. An appropriate therapy event was defined as ATP and shock therapies delivered for ventricular tachycardia and ventricular fibrillation. An inappropriate therapy event was defined as ATP and shock therapies delivered for tachycardia including AF, supraventricular tachycardias, or sinus tachycardia, and device error. The EF was assessed with the biplane Simpson's equation using the apical 4-chamber and 2-chamber views.

Data are presented as mean ± SD. Multiple-group comparisons were obtained by analysis of variance. Categorical data are summarized as frequencies and percentages. Differences in baseline characteristics among patients with S-AF group, C-AF group, and no-AF group were analyzed using unpaired Student t tests. Differences in baseline characteristics among patients with HF hospitalization and without HF hospitalization were analyzed using unpaired Student t tests. The paired Student t test was used to compare continuous data within the subgroups during follow-up. The Kaplan-Meier method was used to analyze the time to the occurrence of the therapy event and HF hospitalization during the follow-up period, which was compared using the log-rank test. The hazard ratio and its confidence intervals were analyzed using unpaired Student t tests. The
estimated using the Cox regression model. $P$ values < .05 were considered statistically significant. All statistical analyses were performed with the JMP 14 software (SAS Institute, Inc., Cary, North Carolina). The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

3 RESULTS

3.1 Patient characteristics

We investigated and analyzed a total of 153 patients with a CRT-D. In our study, S-AF group included 30 (19%) patients, C-AF group included 45 (29%) patients, and no-AF group included 78 (52%) patients. Table 1 shows the baseline characteristics of the patients among three groups. Patients in S-AF group were significantly older than those with in no-AF group ($69 \pm 22$ years vs $64 \pm 15$ years, $P = .04$). The detection of the first episode with S-AF group was significantly longer as compared to those with C-AF group ($74 \pm 58$ day vs $44 \pm 40$ day, $P = .03$). Biventricular pacing with S-AF group was significantly lower as compared to those with no-AF group (subclinical-AF 81% vs clinical-AF 85% vs no-AF 94%, $P = .001$). There was no significant difference with catheter ablation for AF; S-AF group 1(3.3%) vs C-AF group 3 (6.6%). There were no significant differences with drug including beta blockers, ACE-I/ARB, Ca antagonist, digoxin, and amiodarone among three groups.

| TABLE 1 Baseline characteristics among three groups |
|--------------------------------------------------|
| Subclinical AF (n = 30) | Clinical AF (n = 45) | No-AF (n = 78) | $P$ value |
| Age (year) | $69 \pm 22$ | $66 \pm 17$ | $64 \pm 15$ | .04 |
| Male sex - no. (%) | 22 (73%) | 32 (71%) | 60 (76%) | .35 |
| Body mass index | $23 \pm 9$ | $22 \pm 8$ | $23 \pm 7$ | .68 |
| CHADS2 score | $2.2 \pm 1.2$ | $2.3 \pm 1.3$ | $2.2 \pm 1.2$ | .65 |
| Underlying disease -no.(%) | | | | |
| Hypertension | 15 (50%) | 23 (51%) | 44 (56%) | .42 |
| Diabetes mellitus | 10 (33%) | 14 (31%) | 28 (35%) | .43 |
| Prior stroke | 2 (7%) | 5 (11%) | 6 (9%) | .53 |
| Prior myocardial infarction | 7 (23%) | 13 (29%) | 15 (19%) | .27 |
| Ischemic cardiomyopathy | 13 (43%) | 19 (43%) | 26 (33%) | .16 |
| Non-ischemic cardiomyopathy | 17 (57%) | 26 (57%) | 54 (67%) | .22 |
| Paroxysmal AF | 18 (60%) | 16 (36%) | | .15 |
| Persistent AF | 12 (40%) | 29 (44%) | | .12 |
| AF burden (%) | $36 \pm 22$ | $41 \pm 25$ | | .25 |
| Time to detection of the first event | $74 \pm 58$ day | $44 \pm 40$ day | | .03 |
| Primary prevention (ICD) | $20 \pm 67$% | $32 \pm 71$% | $47 \pm 60$% | .35 |
| Secondary prevention (ICD) | $10 \pm 33$% | $13 \pm 29$% | $31 \pm 40$% | .38 |
| Ejection fraction (%) | $26 \pm 22$ | $25 \pm 18$ | $27 \pm 14$ | .31 |
| Left atrial size (mm) | $40 \pm 15$ | $41 \pm 20$ | $37 \pm 18$ | .08 |
| CRT responder-no. (%) | $24 \pm 80$% | $36 \pm 80$% | $62 \pm 79$% | .56 |
| PVC burden/24 hr | $0.5 \pm 0.3$ | $0.6 \pm 0.4$ | $0.4 \pm 0.6$ | .45 |
| Biventricular pacing (%) | $81 \pm 13$ | $85 \pm 6$ | $94 \pm 7$ | .001 |
| Mode switch (number of times) | $18 \pm 11$ | $10 \pm 6$ | $0.2 \pm 0.7$ | .001 |
| Catheter ablation for AF* | 1 (3.3%) | 3 (6.6%) | | .22 |
| Medication- no. (%) | | | | |
| Beta-blocker | $24 \pm 80$% | $38 \pm 84$% | $60 \pm 77$% | .15 |
| ACE-I/ARB | $18 \pm 60$% | $29 \pm 64$% | $52 \pm 66$% | .45 |
| Ca antagonist | $3 \pm 10$% | $5 \pm 11$% | $7 \pm 9$% | .45 |
| Diuretics | $27 \pm 90$% | $41 \pm 91$% | $74 \pm 95$% | .32 |
| Digoxin | $3 \pm 10$% | $6 \pm 13$% | $7 \pm 9$% | .41 |
| Amiodarone | $4 \pm 13$% | $7 \pm 16$% | $13 \pm 16$% | .52 |

Abbreviations: ACE, angiotensin converting enzyme; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; CRT, cardiac resynchronization therapy; ICD, implantable cardioverter defibrillator.

*Catheter ablation for AF was performed after device implant.
3.2 | Clinical outcomes

Table 2 shows the clinical outcomes after device implantation. Patients in S-AF group had a higher rate of HF hospitalization as compared with C-AF group and no-AF group (70% vs 49% vs 38%, \( P = .03 \)). Patients with S-AF had a 2-fold higher rate of HF hospitalization as compared with no-AF patients. S-AF group presented with inappropriate therapy more frequently as compared with no-AF group (13% vs 7.7%, \( P = .04 \)). There were no significant differences with stroke or myocardial infarction among three groups. Figure 1 shows the Kaplan–Meier curve for HF hospitalization among three groups. HF with S-AF group had a significantly higher prevalence of HF as compared with C-AF and no-AF group (\( P = .03 \) by log-rank).

3.3 | Number of appropriate and inappropriate ICD therapies

In S-AF group (n = 30), 3 (10%) patients had appropriate therapies and 4 (13%) patients had inappropriate therapies. In C-AF group (n = 45), 3 (8.8%) patients had appropriate therapies and 4 (8.9%) patients had inappropriate therapies. In no-AF group (n = 78), 11 (14%) patients had appropriate therapies and 6 (7.7%) patients had inappropriate therapies. Patients in no-AF group tended to present with appropriate therapies more than in C-AF group.

3.4 | Predictors of HF

Table 3 presented a comparison of the baseline characteristics between HF group and no-HF group. Cardiac rehabilitation without HF group tended to be more frequently as compared to those with HF group (35% vs 27%, \( P = .08 \)). Patients with HF presented with S-AF more frequently as compared in patients without HF (28% vs 11%, \( P = .009 \)). The biventricular pacing in HF group was significantly lower than in no-HF group (84% vs 92%, \( P = .01 \)). The mode switch rate in HF group was significantly higher than in no-HF group (8.1 times vs 4.3 times, \( P = .03 \)). In the multivariate analysis (Table 4), when comparing HF group and no-HF group, the independent predictor for HF hospitalization was presence of S-AF (hazard ratio; 4.47, confidence interval; 1.43-7.52, \( P = .01 \)).

4 | DISCUSSION

4.1 | Main findings

This study showed the relationship between S-AF and HF hospitalization in patients with CRT-D implantation. S-AF was found to be an independent predictor for HF hospitalization. Patients with S-AF presented with inappropriate therapy more frequently as compared to those with no-AF group.

4.2 | Detection of S-AF and relationship between S-AF and stroke

Previous studies have reported that the rate of device-detected S-AF is about 10%10,11. In our study, the rate of device-reported S-AF was high (19.6%), because all patients had a low EF with CRT-D and the...

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**TABLE 2** Clinical outcomes after device implantation

|                  | Subclinical AF | Clinical AF | No-AF | \( P \) value |
|------------------|----------------|-------------|-------|--------------|
| No.%             | 30             | 45          | 78    |              |
| Heart failure-no, (%) | 21 (70%)       | 22 (49%)    | 30 (38%) | .03         |
| Stroke/TIA-no,(%)  | 5 (17%)        | 5 (11%)     | 9 (12%) | .18         |
| Myocardial infarction-no,(%) | 2 (6.7%)   | 3 (6.7%)    | 5 (6.4%) | .73         |
| Device therapy-no,(%) |       |             |       |              |
| Appropriate therapy | 3 (10%)       | 3 (8.8%)    | 11 (14%) | .08         |
| Inappropriate therapy | 4 (13%)      | 4 (8.9%)    | 6 (7.7%) | .04         |

Note: Appropriate therapy, shock and/or anti-tachycardia pacing due to ventricular arrhythmias; inappropriate therapy, shock and/or anti-tachycardia pacing due to AF/AT or sinus tachycardia. Abbreviation: AF, atrial fibrillation.
The follow-up period was long. Mahajan et al reported the figure of seven studies consisting of a total of 15,353 patients, and there was a significant association between S-AF and stroke, with an average odds ratio of 2.41. However, there was no significant relationship between S-AF and stroke event, because our study was small with only 153 patients included.

### 4.3 Relationship between S-AF and HF hospitalization

The ASSERT study did not find a significant relationship between S-AF and HF. In that study, patients had a pacemaker or ICD. On the contrary, the result of our study indicated a significant relationship between S-AF and HF hospitalization. Because patients in our study had a low EF and all patients had CRT-D. Furthermore, a decrease in biventricular pacing might affect for HF hospitalization. Nakajima et al described a significant proportion of the patients developed HF due to an AF episode itself, even among CRT responders. Once AF

| Variable                        | HR   | CI      | P value |
|---------------------------------|------|---------|---------|
| Ejection fraction (<30%)        | 0.65 | 0.31-1.35 | .32     |
| Cardiac rehabilitation          | 1.97 | 0.95-4.05 | .09     |
| Hyperlipidemia                  | 1.51 | 0.88-2.74 | .25     |
| ARB/ACE-I                       | 0.66 | 0.35-1.11 | .12     |
| Subclinical-AF                  | 4.47 | 1.43-13.9 | .01     |
| Biventricular pacing (<85%)    | 1.95 | 0.66-2.56 | .08     |
| Mode switch/3 month (>10)       | 0.61 | 0.22-1.59 | .31     |

**TABLE 3** Baseline characteristics of patients with and without heart failure after device implantation

|                      | Heart failure (+) | Heart failure (−) | P value |
|----------------------|-------------------|-------------------|---------|
| Number               | 73                | 80                | .82     |
| Age (year)           | 66 ± 12           | 65 ± 15           | .84     |
| Male sex – no. (%)   | 53 (73%)          | 59 (74%)          | .22     |
| Body mass index      | 24 ± 11           | 21 ± 8            | .32     |
| CHADS2 score         | 2.3 ± 1.5         | 2.1 ± 1.4         | .32     |
| Underlying disease –no. (%) |        |                   |         |
| Hypertension          | 40 (54%)          | 41 (51%)          | .68     |
| Diabetes mellitus     | 26 (35%)          | 26 (32%)          | .43     |
| Hyperlipidemia        | 47 (64%)          | 42 (52%)          | .06     |
| Chronic kidney disease| 35 (48%)          | 39 (49%)          | .88     |
| Ischemic cardiomyopathy| 27 (37%)         | 31 (39%)          | .58     |
| Ejection fraction (%) | 25 ± 5            | 28 ± 9            | .12     |
| Cardiac rehabilitation| 20 (27%)          | 28 (35%)          | .08     |
| Subclinical AF        | 21 (28%)          | 9 (11%)           | .009    |
| Device therapy        |                   |                   |         |
| Appropriate therapy -no. (%) | 8 (11%)        | 9 (11%)           | .82     |
| Inappropriate therapy -no. (%) | 7 (10%)        | 7 (9%)            | .42     |
| CRT Responder -no. (%) | 62 (85%)         | 60 (75%)          | .26     |
| PVC burden/24-hours   | 0.6 ± 0.5         | 0.4 ± 0.3         | .52     |
| Biventricular pacing (%) | 84%              | 92%               | .01     |
| Mode switch           | 8.1 ± 10          | 4.3 ± 4           | .03     |
| Catheter ablation for AF*| 2 (2.7%)       | 2 (2.5%)          | .72     |
| Medication- no. (%)   |                   |                   |         |
| Beta-blocker          | 60 (82%)          | 62 (78%)          | .88     |
| ACE-I/ARB             | 45 (61%)          | 54 (67%)          | .12     |
| Ca antagonist         | 7 (10%)           | 8 (10%)           | .82     |
| Diuretics             | 69 (95%)          | 73 (91%)          | .22     |
| Digoxin               | 7 (10%)           | 9 (11%)           | .56     |
| Amiodarone            | 10 (14%)          | 14 (18%)          | .35     |

**TABLE 4** Multivariate analysis of heart failure

Abbreviations: ACE, angiotensin converting enzyme; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; CRT, cardiac resynchronization therapy.

*Catheter ablation for AF was performed after device implant.
occurred, the biventricular pacing decreased significantly, and the patients who had a lower biventricular pacing during periods of AF exhibited a worse clinical outcome.

Furthermore, patients with AF and a biventricular pacing <90% had a higher incidence of HF or death than both the patients with an AF and biventricular pacing ≥90% and those with SR.

Another study reported that AF in CRT patients was associated with an increase in HF hospitalization and death, mainly because uncontrolled ventricular rates reduce the delivery of an optimal biventricular pacing. A biventricular pacing <90% was associated with a higher incidence of HF and death, and a biventricular pacing >98% significantly reduced HF and death. In our study, the biventricular pacing in the S-AF group was significantly lower as compared with no-AF group (81% vs 94%). Previous studies have described AF patients as S-AF with C-AF, whereas our study divided patients into the S-AF or C-AF group. This classification is important for HF in patients receiving CRT-D. In patients with C-AF, the ventricular rate can be controlled and the SR returned using medication. On the other hand, patients with S-AF had no symptoms and time to the detection of the first episode was late.

Therefore, the biventricular pacing in the S-AF group was low and the decrease of biventricular pacing might affect an increased incidence of HF hospitalization. Frequent PVCs might affect the biventricular pacing and might affect HF hospitalization. However, there was no significant difference with PVC burden by 24 hours monitoring among three groups. In this study, data was evaluated after CRT-D implant. Therefore, PVC burden had little effect on the biventricular pacing. It appeared that patients with S-AF had less biventricular pacing due to AF. One potential of the mechanism underling AF progression with HF might be the inability of patients predisposed to HF to tolerate prolonged, rapid ventricular rates during S-AF, leading to the clinical unmasking of HF. Furthermore, tachycardia induced cardiomyopathy due to prolonged episodes of S-AF may be an important factor in some patients. Atrial systole constitutes a considerable proportion of the cardiac output in patients predisposed to HF, and its loss during episodes of S-AF might also account for some of the observed increase in HF risk.

Nishinari et al reported that in patients without clinical AF who had a cardiac device, new-onset atrial high-rate episode identified as asymptomatic AF was detected in 32.7% of the patients during the first year after implantation of the cardiac device. Furthermore, a higher atrial high-rate episode burden was more strongly associated with future risk of worsening HF in patients with a cardiac device. These studies emphasized the importance of early detection of AF for predicting clinical HF. Thus, it is important with early S-AF detection for preventing HF hospitalization. Catheter ablation for AF and amiodarone might affect the clinical event such as ICD therapy as well as HF hospitalization. However, there was no significant difference with catheter ablation and amiodarone in our study.

4.4 Inappropriate therapy induced by S-AF

Previous study reported that the rate of inappropriate therapy was 13% in patients without AF, 28% in patients with paroxysmal AF, 18% in patients with persistent AF and 32% in patients with permanent AF. In the no-AF group, new-onset AF during follow-up was the cause of inappropriate device shocks in 27(4%) patients. We described that 4 (13%) in patients with S-AF had inappropriate therapies, 4 (8.9%) in patients with C-AF had inappropriate therapies, and 6 (7.7%) in patients without AF had inappropriate therapies. The data by Borleffs et al included patients with a history of AF, on the other hand, our data excluded patients with a history of AF. Other studies demonstrated the relationship between the existence of AF and inappropriate device discharge. In addition, they also reported the consequence negative effects of inappropriate device discharge on patient quality of life and demonstrated the impact of inappropriate shock delivery on mortality. Poole et al also reported that the occurrence of inappropriate ICD shock was associated with a significant increase in the risk of death as compared with no inappropriate shock. The most common cause of death among patients who received any ICD shock was progressive HF. On the other hand, there was no relationship between AF and mortality in our study. Our data excluded patients with a history of AF and contained only a small number of patients. However, there was a significant relationship between S-AF and HF hospitalization, and our finding show that inappropriate therapy might affect the HF hospitalization in patients with S-AF.

5 LIMITATIONS

The study has several limitations. First, this study was a retrospective nonrandomized, single-center study and the decision to implant a CRT device was likely based on multiple factors. Second, this study had a small number of patients, and the results therefore must be interpreted with caution. However, we believe that this study is an adequate evaluation as we found a significant association between S-AF and HF hospitalization. Third, S-AF was defined as AF was received any ICD shock was progressive HF. On the other hand, there was no relationship between AF and mortality in our study. Our data excluded patients with a history of AF and contained only a small number of patients. However, there was a significant relationship between S-AF and HF hospitalization. Further studies will be required to be certain the relationship between S-AF and HF hospitalization.

6 CONCLUSIONS

S-AF after CRT-D implantation was associated with a significantly increased risk of HF hospitalization. The loss of the biventricular pacing and increasing an inappropriate therapy might affect the risk of HF hospitalization.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.
DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES
1. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic use of an implanted defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med. 2002;346:877-883.
2. Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004;350:2140-2150.
3. Cleland JG, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med. 2005;352:1539-1549.
4. Hayes DL, Boehmer JP, Day JD, et al. Cardiac resynchronization therapy and the relationship of percent biventricular pacing to symptoms and survival. Heart Rhythm. 2011;8:1469-1475.
5. Koplan BA, Kaplan AJ, Weiner S, Jones PW, Seth M, Christman SA. Heart failure decompensation and all-cause mortality in relation to percent biventricular pacing in patients with heart failure: is a goal of 100% biventricular pacing necessary? J Am Coll Cardiol. 2009;53:355-360.
6. Ruwald AC, Kutyifa V, Ruwald MH, et al. The association between biventricular pacing and cardiac resynchronization therapy-defibrillator efficacy when compared with implantable cardioverter defibrillator on outcomes and reverse remodelling. Eur Heart J. 2015;36:440-448.
7. Mittal S, Musat DL, Hoskins MH, et al. Clinical outcomes after ablation of the AV junction in patients with atrial fibrillation: impact of cardiac resynchronization therapy. J Am Heart Assoc. 2017;6:e007270.
8. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Europace. 2016;18(11):1609-1678.
9. Kirchhof P, Breithardt G, Aliot E, et al. Personalized management of atrial fibrillation: proceedings from the fourth atrial fibrillation competence NET work/European heart rhythm association consensus conference. Europace. 2013;15(11):1540-1556.
10. Healey JS, Connolly SJ, Gold MR, et al. Subclinical atrial fibrillation and the risk of stroke. N Engl J Med. 2012;366(2):120-129.
11. Van Gelder IC, Healey JS, Crijns HJGM, et al. Duration of device-detected subclinical atrial fibrillation and occurrence of stroke in ASSERT. Eur Heart J. 2017;38(17):1339-1344.
12. Mahajan R, Perera T, Elliott AD, et al. Subclinical device-detected atrial fibrillation and stroke risk: a systematic review and meta-analysis. Eur Heart J. 2018;39(16):1407-1415.
13. Nakajima I, Noda T, Kanazaki H, et al. Development of heart failure from transient atrial fibrillation attacks in responders to cardiac resynchronization therapy. JACC Clin Electrophysiol. 2018;4(9):1227-1234.
14. Borleffs CJ, van Rees JB, van Welsenes GH, et al. Prognostic importance of atrial fibrillation in implantable cardioverter-defibrillator patients. J Am Coll Cardiol. 2010;55(9):879-885.
15. Daubert JP, Zareba W, Cannom DS, et al. Inappropriate implantable cardioverter-defibrillator shocks in MADIT II: frequency, mechanisms, predictors, and survival impact. J Am Coll Cardiol. 2008;51:1357-1365.
16. Mark DB, Anstrom KJ, Sun JL, et al. Quality of life with defibrillator therapy or amiodarone in heart failure. N Engl J Med. 2008;359:1009-1008.
17. Poole JE, Johnson GW, Hellkamp AS, et al. Prognostic importance of defibrillator shocks in patients with heart failure. N Engl J Med. 2008;359:1009-1017.

How to cite this article: Arai S, Kawamura M, Gokan T, et al. Relationship between device-detected subclinical atrial fibrillation and heart failure in patients with cardiac resynchronization therapy defibrillator. Clin Cardiol. 2020;43:1517-1523. https://doi.org/10.1002/clc.23471