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Diagnostic usefulness of implantable loop recorder in patients with unexplained syncope or palpitation

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Abstract

Background: In a substantial proportion of patients with syncope, the exact cause is not identified because of the difficulty to document electrocardiograms correlated with the events during a syncope episode. Thus, an implantable loop recorder (ILR) was introduced for diagnosing hidden arrhythmia; however, its clinical use remains limited. Therefore, we conducted a retrospective analysis to assess the diagnostic value of the ILR in patients with unexplained syncope or palpitations.

Methods: All patients who had undergone ILR implantation from May 2016 to January 2020, were studied retrospectively. We analyzed their electrocardiogram stored in the device.

Results: Among the 70 patients (mean age ± SD; 50.2 ± 20.3 years, 27 men) with unknown causes of syncope or palpitation, during two years follow-up, arrhythmia was detected in 26 patients (37.1%). Nineteen (73.1%) patients underwent permanent pacemaker implantation due to symptomatic bradycardia or atrioventricular block. All arrhythmias were detected within 6 days to 39 months after loop recorder implantation. Thirteen patients (50%) showed sick sinus syndrome (eight long pauses and five tachycardia-bradycardia syndromes). Eleven patients (42.3%) had paroxysmal atrioventricular block. Two patients who underwent permanent pacemaker implantation showed a positive tilt-table test. Three patients underwent radiofrequency catheter ablation for paroxysmal supraventricular tachycardia and atrial fibrillation. The mean duration for the detection of first sign (arrhythmia or palpitations) was 7.5 months, and the time from the detection of arrhythmia to ablation or device implantation was 3.4 months.

Conclusion: ILR monitoring detected a substantial number of significant bradycardias in patients with unexplained syncope and palpitations, suggesting that it is an effective diagnostic method that can shorten the time required to identify the cause of arrhythmias.

Keywords: Implantable loop recorder, Syncope, Pacemaker implantation

Introduction

Syncope is a common clinical symptom in all age groups and is defined as non-traumatic transient loss of consciousness [1]. The most common cause of syncope is reflex syncope (21%), followed by cardiac-induced syncope (9%) and orthostatic hypotension (9%). However, unknown causes account for 37% of syncope cases [2]. Although syncope has a relatively good prognosis, it can

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be fatal if not treated properly. However, the exact cause of syncope or pre-syncope cannot be determined because it is difficult to document the correlation between electrocardiograms (ECG) and the events. Therefore, if the cause of syncope is unclear after a noninvasive examination, additional evaluation is necessary. According to the European Society of Cardiology (ESC) guidelines (2018), an implantable loop recorder (ILR) is recommended in Class-I level of evidence[1]. The ESC guidelines recommend an implantable event recorder for an early stage evaluation of syncope of unknown cause in patients who are not at high risk and who are likely to recur within battery life (approximately 3 years) [3]. The ILR was first introduced in 1990 [4]. In South Korea, the ILR has been introduced into clinical practice since 2006 and has been used for diagnostic purposes in patients with unexplained syncope or palpitations. Although ILR has been introduced for the diagnosis of hidden arrhythmias, which are usually difficult to diagnose, its clinical use is still limited because it is an invasive evaluation and the detection and treatment period of arrhythmias using it are not well known. Therefore, we sought to evaluate the diagnostic value of the ILR in patients with syncope or palpitations of unknown etiology, and the time to diagnose and treat arrhythmias after loop recorder implantation.

Methods

Study subjects and design

Consecutive patients who underwent ILR implantation from May 2016 to January 2020 were retrospectively analyzed. The Institutional Review Board of the Korea University Anam Hospital (No. 2018AN0038) approved the study protocol, and written consent was obtained from all eligible participants prior to enrollment. Initial evaluations included history collection, physical examination, and a baseline 12-lead ECG. Additional evaluations included transthoracic echocardiography, exercise stress test, tilt-table test, orthostatic blood pressure measurement, and 24-h Holter monitoring if necessary. Among them, 24-h Holter monitoring was performed in all patients, and if clinically necessary, an electrophysiological study or coronary angiography was performed. The 2017 American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines and 2018 ESC guidelines were referred for syncope assessment [1, 5].

ILR implantation and follow-up

The patients had a loop recorder implanted (63 patients; Reveal LINQ™ Insertable Cardiac Monitor, Reela Plusor Reveal DX-XT; Medtronic Inc., Minneapolis, MN, USA and 3 patients; Confirm™, St. Jude Medical, St. Paul, MN, USA) in our hospital. The loop recorder was placed subcutaneously in the left pectoral region next to the nipple line of the patient under local anesthesia. Subsequently, an incision of approximately 1–2 cm was made in the skin on the left chest pectoral area that extended approximately 5 cm subcutaneously (Additional File 1: Supplementary Figure S1). After the pocket was made, the loop recorder was implanted with the front side up under fluoroscopy, and the skin was sutured after checking for hemorrhage. The procedure was completed after compression dressing. At the end of the procedure, the gain and sensitivity were set and a programmer was used to follow the threshold, longevity, impedance, and sensitivity. There are two methods for storing the ECG in the ILR: an automatic activation method that automatically recognizes and records arrhythmias and a patient-activation method that records arrhythmias by activating a portable activator when the patient has symptoms. In the outpatient clinic, regular ILR interrogations were performed every 3–6 months, at the discretion of the physician. If the patient had cardiac symptoms, such as palpitation, dizziness, or syncope, ILR interrogation was performed immediately. The ILR interrogations were automatically performed and validated by an electrophysiological cardiologist. False episodes were classified as pseudopauses, noises, artifacts, under sensing, and signal over sensing.

Outcomes measurements

The primary outcome was the documentation of symptom-related arrhythmias. Arrhythmias were defined as atrial fibrillation (AF), narrow QRS tachycardia, wide QRS tachycardia, sick sinus syndrome (SSS), tachycardia-bradycardia syndrome (TBS), or atrioventricular (AV) block. The secondary outcomes were the evaluation of the time taken to diagnose arrhythmias after implantation of the loop recorder and the time taken to perform ablations or device implantations after the detection of arrhythmias.

Statistical analysis

Continuous variables were summarized as standard deviations and means or medians. An independent *t*-test was used to compare continuous variables, and Mann–Whitney U test was performed for comparing the nonparametric data. Histograms were used for continuous measurements and to understand the distribution of values. All *p*-values were reported as 2-tailed, and statistical significance was considered at $p < 0.05$. Statistical analyses were performed using SPSS (version 24.0; SPSS Inc., Chicago, IL, USA).

Result

Clinical characteristics

We assessed 70 patients who underwent loop recorder implantations for unexplained syncope or palpitations between May 2016 and January 2020. Of these, 26 (36%) patients were documented to have significant arrhythmias in ILR interrogation of symptoms. Four (15.4%) patients underwent radiofrequency catheter ablation (RFCA) or cryoballoon ablation for paroxysmal AF and supraventricular tachycardia. Nineteen (73.1%) patients underwent permanent pacemaker implantations for SSS, TBS, and paroxysmal AV block. Of the patients with arrhythmias, three (11.5%) were followed up without management (Fig. 1).

Compared with patients without documented arrhythmias, those patients with arrhythmias were significantly older (57.3 ± 18 vs. 46 ± 20.6 years, $p = 0.023$). Men were more affected than women (53.8% vs. 29.5%, $p = 0.444$). Two (7.7%) patients with arrhythmias and six (13.6%) without arrhythmias underwent RFCA before loop recorder implantation, but the difference was not statistically significant. Left ventricular ejection fraction was similar in both the groups (Table 1).

Arrhythmia detection and performance of correction procedures

All patients underwent noninvasive arrhythmia monitoring with 24-hour ambulatory Holter monitoring or 30 days of event recording prior to loop recorder implantation. The episodes monitored included syncope, pre-syncope or palpitations. Pre-syncope was defined as faintness, dizziness, or light-headedness (Additional File 1: Supplementary Table S1). The mean number of episodes was 2.4. During the diagnostic work-up, the tilt-table tests and electrophysiological studies were performed in 30% and 34.6% patients, respectively. Two patients showed positive response during the tilt-table test (Table 2). Table 3 shows the arrhythmias documented during the follow-up period. The mean time taken for the occurrence of the first event was 7.5 ± 9.5 months; 19 (73%) patients were implanted with permanent pacemakers, and four (15.4%) underwent RFCA or cryoballoon ablation. Seven patients, who received pacemakers (PM) for SSS (29%), TBS (57%), and paroxysmal AV block (14%), had a history of PAF prior to loop recorder implantation.

Most of the patients were symptomatic when arrhythmias were documented. A 68-year-old man experienced pre-syncope symptoms, and a paroxysmal AV block was documented in ILR interrogation. An 81-year-old woman had several episodes of syncope. The ILR showed sinus pause for 6.4 s with dizziness. A 74-year-old woman presented to our hospital with palpitations and dizziness. ILR showed narrow QRS tachycardia. The EPS showed atrioventricular nodal reentrant tachycardia. Therefore, slow pathway ablation was performed. A 79-year-old woman experienced pre-syncope after tachycardia. She had a history of paroxysmal AF, and TBS was detected in ILR interrogation with a maximum RR interval of 6 s (Fig. 2).

The mean duration of time taken to diagnose arrhythmia after loop recorder implantation was

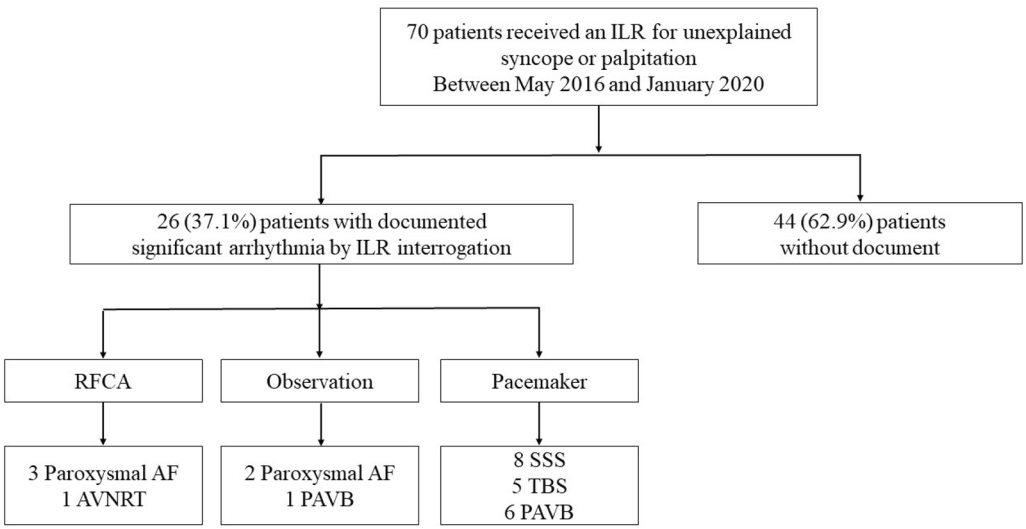

Fig. 1 Study Flow. Flowchart showing the study design and further management of patients who received ILR. ILR, implantable loop recorder; AF, atrial fibrillation; AVNRT, atrioventricular nodal reentry tachycardia; PAVB, paroxysmal atrioventricular block; SSS, sick sinus syndrome; TBS, tachycardia-bradycardia syndrome; RFCA, radiofrequency catheter ablation

Table 1 Baseline characteristics of patients with documented arrhythmia by implantable loop recorder (ILR) and not documented arrhythmia

Variables	Arrhythmia detected (n = 26)	No arrhythmia detected (n = 44)	*p*-value
Age (years)	57.3 ± 18	46 ± 20.6	0.023
Men, n (%)	14 (53.8)	13 (29.5)	0.044
Body weight (kg)	63.7 ± 14.3	64.7 ± 12.8	0.746
Height (cm)	161.6 ± 11.9	168.1 ± 9.4	0.014
BMI (kg/m^2)	24.1 ± 3.2	22.9 ± 4.0	0.173
Hypertension, n (%)	6 (23.1)	7 (15.9)	0.456
Diabetes mellitus, n (%)	1 (3.8)	2 (4.5)	0.889
Previous stroke, n (%)	2 (7.7)	0 (0)	0.062
Other arrhythmias, n (%)	5 (33.8)	12 (27.3)	0.448
Structural heart disease, n (%)	4 (15.4)	3 (6.8)	0.248
Previous RFCA, n (%)	2 (7.7)	6 (13.6)	0.450
Left ventricular ejection fraction (%)	57.7 ± 1.5	56.1 ± 3.0	0.017
Left atrium diameter (mm)	37.2 ± 7.2	34.9 ± 5.7	0.142

BMI, body mass index; RFCA, radiofrequency catheter ablation

Table 2 Diagnostic work up

Patient	Sex/age	Prior arrhythmia	Episodes	Treadmill test	Tilt-table test	EPS
1	M/43	None	1	Negative	None	Yes
2	F/69	Paroxysmal AF	1	None	None	None
3	F/79	Paroxysmal AF	3	Inappropriate	None	None
4	M/46	None	1	Negative	Negative	Yes
5	F/61	None	1	None	None	Yes
6	M/68	None	3	Negative	None	None
7	F/81	None	2	Negative	None	None
8	M/65	None	1	Inappropriate	None	None
9	M/80	Paroxysmal AF	2	None	Positive	None
10	M/69	RFCA for PAF	1	None	Negative	None
11	M/70	None	6	Negative	Negative	Yes
12	F/51	Paroxysmal AF	5	Negative	None	None
13	F/75	None	1	Inappropriate	None	None
14	F/82	Paroxysmal AF	1	None	Negative	None
15	M/55	None	4	Negative	Negative	None
16	F/47	None	4	Negative	None	None
17	M/43	None	2	Negative	None	Yes
18	M/70	Paroxysmal AF	1	None	None	None
19	M/23	None	1	Negative	Positive	Yes
20	F/40	None	6	None	None	None
21	F/74	None	2	None	None	Yes
22	F/28	None	5	Negative	None	None
23	F/59	Paroxysmal AF	2	Negative	None	None
24	M/38	None	1	Negative	None	Yes
25	M/23	None	1	Negative	Negative	Yes
26	F/52	None	5	Negative	None	None

AF, atrial fibrillation; M, male; F, female; RFCA, radiofrequency catheter ablation; EPS, electrophysiological study; PAF,

Table 3 Documented arrhythmia during follow-up

Patient	First event (days)	Finding on ILR	Management
1	572	SSS	Permanent pacemaker
2	34	SSS	Permanent pacemaker
3	193	TBS	Permanent pacemaker
4	104	PAVB	Permanent pacemaker
5	1188	SSS	Permanent pacemaker
6	78	High degree AVB	Permanent pacemaker
7	101	TBS	Permanent pacemaker
8	6	PAVB	Permanent pacemaker
9	340	TBS	Permanent pacemaker
10	21	PAVB	Permanent pacemaker
11	34	SSS	Permanent pacemaker
12	138	SSS	Permanent pacemaker
13	893	SSS	Permanent pacemaker
14	11	TBS	Permanent pacemaker
15	120	PAVB	Permanent pacemaker
16	323	SSS	Permanent pacemaker
17	92	PAVB	Permanent pacemaker
18	76	TBS	Permanent pacemaker
19	107	SSS	Permanent pacemaker
20	429	Paroxysmal AF	RFCA
21	15	AVNRT	RFCA
22	409	PAVB	Observation
23	337	Paroxysmal AF	Cryoballoon ablation
24	61	Paroxysmal AF	Observation
25	108	Paroxysmal AF	Observation
26	49	Paroxysmal AF	RFCA

SSS, sick sinus syndrome; TBS, tachycardia-bradycardia syndrome; PAVB, paroxysmal atrioventricular block; AF, atrial fibrillation; RFCA, radiofrequency catheter ablation; ILR, implantable loop recorder; AVNRT, atrioventricular nodal reentry tachycardia

7.5 ± 9.6 months. Furthermore, the mean duration of time taken to perform therapeutic interventions after arrhythmia detection was 3.4 ± 5.8 months (Fig. 3).

Discussion

The main findings of this study in patients with ILR were as follows: ILR interrogation revealed significant arrhythmias in 25 patients (37%), of whom 19 (73.1%) had a permanent pacemaker implanted. Other patients with arrhythmias detected on ILR were treated effectively with RFCA, cryoballoon ablation, and medication. The mean time taken for arrhythmia detection after implantation of the loop recorder was 7.5 ± 9.6 months. The mean time taken to initiate management after arrhythmia detection was 3.4 ± 5.8 months. The mean time from arrhythmia detection to permanent pacemaker implantation was 2.3 months, and the mean time taken to undergo RFCA or cryoballoon ablation was 10.8 months. Actual syncope detection rates may be as low as 1–2%, as most of the episodes do not recur during 24-hour Holter monitoring [6]. Event recorders and wearable watches may be useful in the investigation of palpitations, but difficulties in obtaining an ECG at the moment of an episode may limit the assessment of syncope [7]. Sulke et al.[8] reported that 23% of patients with ILR had bradycardia indications requiring a permanent pacemaker, while only 3% of patients who had undergone conventional management had bradycardia. In addition, the ECG diagnosis time of patients with ILR was significantly shorter than that of conventionally managed patients.

In this study, the detection rate of arrhythmia was 37%; however, among them, patients with permanent pacemakers showed a high rate (73.1%). This indicates that ILR can better detect severe bradycardia or atrioventricular block in patients with syncope of unknown cause and appropriate treatment strategy can be selected for them. In some previous studies, among patients with significant arrhythmias detected by ILR, 34.7% had a permanent pacemaker and 2.9% had an intracardiac defibrillator [9]. However, significant arrhythmias were found in 37% of patients over a period of approximately 7.5 months in our study. This was found within a shorter period of time when compared with the time taken to detect arrhythmias in other studies (20% detection in six months and 30% in one year) [10]. Furukawa et al. [11] reported that when patients with ILR were observed for four years, the cumulative incidence of arrhythmias gradually increased from 30% in the first year to 80% in the fourth year. Farwell et al. [12] reported that treatment based on ILR diagnosis significantly reduced syncope recurrence when compared to treatment based on conventional diagnostic methods. Secondary syncope was observed in 16.4% of patients who received conventional treatment, and 9.1% of those who received ILR [11]. This shows that the ILR plays an important role in determining a more appropriate treatment method. The ILR is also cost-effective. Although that study was evaluated in Europe, Giada et al. [13] and Krahn et al. [14] showed that the average cost for the primary evaluation of arrhythmias in patients with unexplained syncope or palpitation was significantly lower in ILR patients than in the conventional diagnostic group. In clinical practice, assessing syncope whenever symptoms occur in patients with unknown causes can be more expensive than performing continuous follow-up after the implantation of a loop recorder.

According to previous insurance standards in Korea, the ILR was only eligible for insurance benefits if the cause could not be found after the syncope evaluation. However, since July 1, 2016, the criteria for recognition of insurance benefits have been expanded, and a new

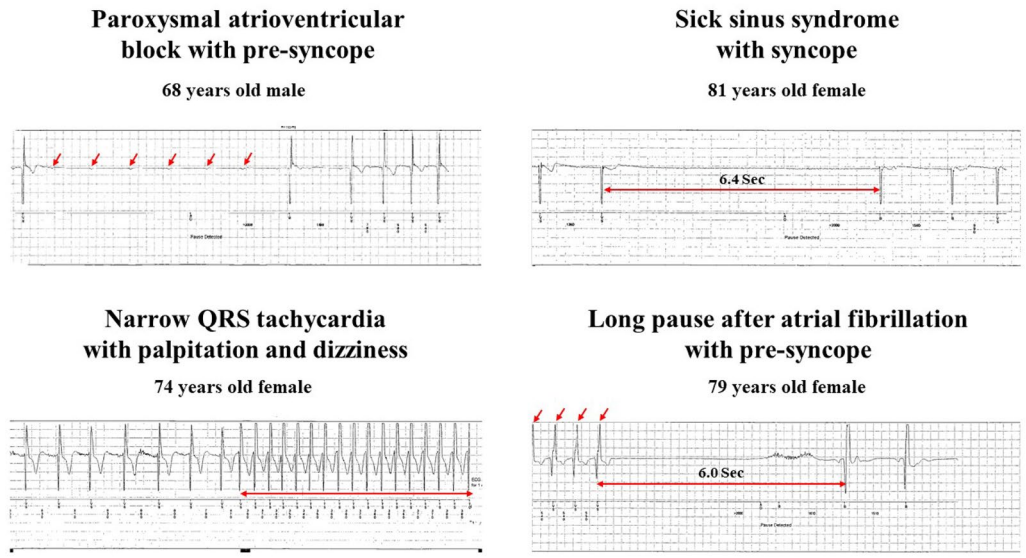

Fig. 2 Representative examples of arrhythmias that were detected in the tracings downloaded from the ILR at the time of symptoms

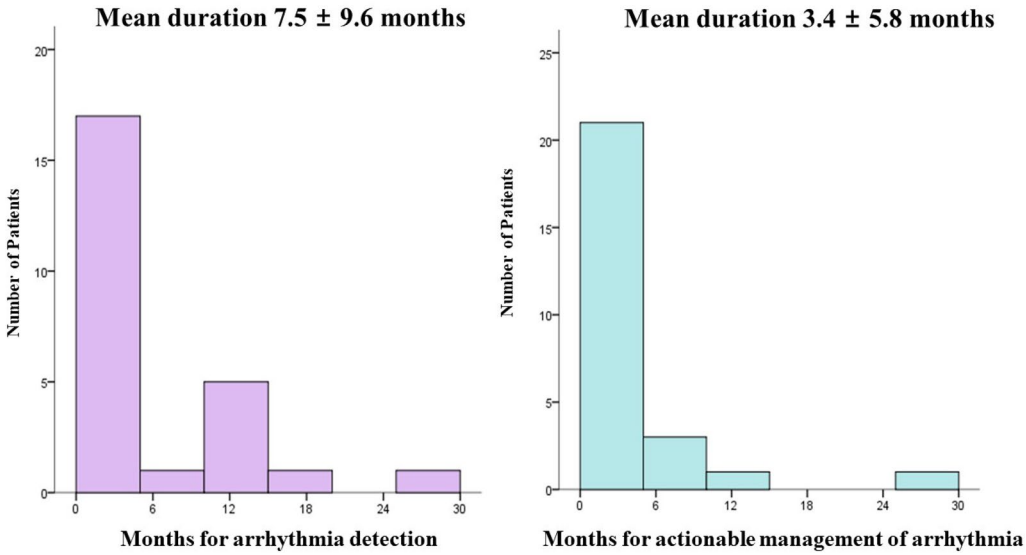

Fig. 3 Time duration for the detection and treatment of arrhythmia. The histograms show the mean duration of time from implantation of the loop recorder to the diagnosis of arrhythmias and the mean duration from arrhythmia detection to treatment initiation

insurance standard is available that covers patients with recurrent stroke that is suspected to be atrial fibrillation, which was not observed in other tests, recurrent syncope, or recurrent palpitations. In addition, in patients with structural heart disease, insurance coverage is available for even one episode of syncope. As the range of indications in which loop recorders can be implanted expand, patient access to treatment improves.

ILR reduces unnecessary investigations and hospitalizations of patients to determine the cause of syncope or palpitations, thereby, lowering the associated costs. It increases the diagnostic rate of arrhythmias and thus helps in providing appropriate treatment to patients. According to the current revised ESC guidelines, ILR is recommended in class I: level of evidence A. It is used for the initial evaluation of patients with recurrent syncope of unknown cause, high-risk patients who are not

undergoing syncope treatment, and high-risk patients without primary prevention implantable cardioverter defibrillator or pacemaker indications. ILR implantation is an invasive procedure, and there are no large-scale studies conducted in Asia related to its effectiveness; therefore, it is under-used in Korea.

Limitations

Our study has several limitations. First, this was a single-center retrospective study. Therefore, the number of patients enrolled in this study was small. Second, the mean time from the detection of arrhythmia to treatment was 3 months. The time from the detection of atrioventricular block or severe bradycardia to pacemaker implantation was less than 1 month. RFCA was possible only after taking antiarrhythmic drugs for at least 6 weeks after AF detection; therefore, the time from the detection of arrhythmia to treatment was increased. Third, the mean follow-up period was 21 ± 12.7 months. As with a study in which 80% of arrhythmias were found over 4 years, more symptom-related arrhythmias could have been detected if patients with ILR were followed for a long period of time resulting in more accurate detection and treatment of arrhythmias.

Conclusion

This study showed that ILR monitoring could detect a substantial number of clinically significant tachycardia and bradycardias in patients with unexplained syncope or palpitations, suggesting that it is an effective diagnostic method that shortens the time for identifying arrhythmia cases.

Abbreviations

AF: Atrial fibrillation; AV: Atrioventricular; ECG: Electrocardiogram; ESC: European Society of Cardiology; ILR: Implantable loop recorder; PAF: Paroxysmal atrial fibrillation; PM: Pacemaker; RFCA: Radiofrequency catheter ablation; SSS: Sick sinus syndrome; TBS: Tachycardia-bradycardia syndrome.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s42444-022-00068-w.

Additional file 1. Supplementary Figure S1. ILR location and interrogation.

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Not applicable.

Author contributions

J-I Choi had full access to all the data in this study and takes responsibility for its integrity and analytical accuracy. The concept and design of the study were developed by YY Choi, J-I Choi, and YH Kim. Data analysis and interpretation were performed by YY Choi, YG Kim, KJ Min, SY Rho, J Shim, JS Kim, and J-I Choi. YY Choi and J-I Choi drafted the manuscript. Statistical analyses was performed by YY Choi. All authors have read and approved the final manuscript.

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Availability of data and materials

The data generated during this study are available from the corresponding author(s) upon reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol adhered to the Declaration of Helsinki and was approved by the Institutional Review Board of Korea University Anam Hospital (No. 2018AN0038).

Consent for publication

All authors have permitted the publication.

Competing interests

The authors have no conflicts of interest to disclose.

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