

## Efficacy And Safety Of Implantable Loop Recorder: Experience Of A Center

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### Abstract

**Introduction:** Symptoms like syncope or palpitations frequently present a diagnostic challenge. An implantable loop recorder (ILR) is an important aid in the management of these patients.

**Methods:** A retrospective study of patients that underwent ILR implantation from November 2007 to 2014. For each patient the indication for implantation, baseline characteristics, previous study, complications, recorded tracing and interventions were evaluated.

**Results:** A total of 62 patients were included, 50% men, with a mean age of  $62.5 \pm 18.8$  years old. Previously to ILR implantation 88.7% of patients had performed Holter, 17.7% external events recorder, 33.9% Tilt test and 29% an electrophysiological study. The implantation indications were recurrent syncope in 90.3%, palpitations 8.1% and ischemic stroke in one patient. Mean follow-up time was  $17.1 \pm 16.3$  months. Symptoms were reported in 66.1% of the patients, 46.8% of those yielding a diagnostic finding. In all cases of palpitation complaints with diagnosis we found atrial fibrillation (AF). In patients with syncope atrioventricular conduction disturbance was demonstrated in 19.6%, sinus node dysfunction in 16.1%, paroxysmal supra-ventricular tachycardia 7.1% and AF in 1.8%. These finding resulted in 19 pacemaker and one CRT-D implantation, introduction of anticoagulation in five patients and one ablation of accessory pathway. There were no major complications.

**Conclusion:** ILR proved to be safe and efficient. It has enabled the identification or exclusion of serious rhythm disturbances in more than half of patients and provided a targeted therapeutic intervention.

### Introduction

Symptoms like syncope or palpitations are common conditions in clinical practice, thus having a significant impact on the patient's quality of life. They are frequent causes of cardiology referral and even hospitalization.<sup>1</sup> Due to the variety of underlying possible mechanisms, the precise diagnosis relies on the correlation between symptoms and electrocardiography evidence at the time of episodes. However, given the paroxysmal and unpredictable nature of these symptoms, they frequently present a diagnostic challenge.

The choice of monitoring technique in different clinical situations should be driven by the stratification risk and predicted rate of symptom recurrence.<sup>1,2</sup> Conventional Holter monitoring and external loop recorders are known to have low diagnostic yield, and even after an extensive evaluation many patients remain undiagnosed.<sup>3,4</sup> A long-term monitoring through an implantable loop recorder (ILR)

is an important aid in the management of these patients.

In recent years, significant advances have been made in diagnosing and understanding the mechanisms of rhythm conditions, with an increased number of patients having a final diagnosis. This increment has been greatly enhanced by the development and widespread use of the ILR. It is a small subcutaneous device for continuous electrocardiographic monitoring that can be extremely useful in the diagnosis of syncope of undetermined origin after the initial assessment, in patients with unrecorded palpitations that occur occasionally, in detection of atrial fibrillation and study of cryptogenic stroke.<sup>5</sup> The efficacy and safety of the ILR as a diagnostic tool has already been demonstrated in several studies.<sup>6,7,8</sup>

The aim of this study was to describe the experience of a tertiary center with the use of ILR.

### Material and Methods

A retrospective, observational, single-center study of consecutive patients that underwent ILR implantation during a seven years period. All patients had a Cardiology evaluation and at least a basic study with an ECG and transthoracic echocardiogram previous to the procedure.

We collected clinical and electrocardiographic data from a prospective database and from medical electronic and ILR records.

We used the Reveal DX/XT/LINQ ILR device (Medtronic) a subcutaneously implantable device for long-term continuously

### Key Words:

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cardiac rhythm monitoring for up to three years. The device was subcutaneously implanted in the left parasternal region, under local anesthesia. Events could be recorded by two methods: manually activated by the patients in case of symptoms or automatically triggered when arrhythmic events satisfied the pre-programmed cut-off criteria for asystole, brady or taquiarrhythmias and atria or ventricular fibrillation. Generally, the device memory can automatically store between 27 to 29 automatically activated events with 30 seconds of pre-activation and 27 seconds of post-activation and 3 patient-activated events with 6.5 minutes of pre-activation and 1 minute of post-activation, with few variances according to the type of arrhythmic event and program design. Patients had a first follow-up visit in three months, in six months intervals thereafter, and after every event activated. Sixteen patients had CareLink remote monitoring system that transmits the information of the arrhythmic event or activated episodes at distance to a web server that can be accessed by the assistant doctor or arrhythmic unit staff.

In the present study, the implantation indication, baseline characteristics, study previous to ILR implantation, complications of procedure, recorded monitoring tracings and subsequent interventions, were evaluated for each patient

The statistical analysis was performed with SPSS 20 version.

## Results

Between November 2007 and November 2014 a total of 62 patients were included, 50% were men, with a mean age of  $62.5 \pm 18.8$  years old. The demographic and clinical characteristics of patients are presented in Table 1. All patients had a baseline echocardiogram and ECG, with 95% of the patients in sinus rhythm. QRS complex and atrial ventricular conduction was normal in 63.1% of the patients. 17.3% presented with first degree atrioventricular block, 12.9% had right bundle branch block and 6.7% left bundle branch block. Further ECG characteristics are described in Table 2. In 19.4% structural heart disease was identified and 88.7% of the patients had a normal left ventricular ejection fraction.

Previously to ILR implantation, 88.7% of the patients had performed at least one Holter monitoring, 17.7% an external event recorder, 33.9% a Tilt table test and 29% an electrophysiological study. Thus, 23.3% of patients underwent more than two different types of complementary exams before IRL implantation without a

clear diagnosis.

Regarding the implantation indications, 90.3% were for recurrent syncope/presyncope, 8.1% for palpitations complaints and in one case, ischemic stroke with suspected cardioembolic origin after initial assessment. Mean follow-up time was  $17.1 \pm 16.3$  months (IQR 4-30). During follow-up, symptoms were reported in 66.1% (n=41) of the patients and from those, 29 (46.8%) yielded a diagnostic finding (44.5% of the patients with syncope, 60% of patients with palpitations symptoms and in the ischemic stroke case), with a mean time of  $12.8 \pm 14.4$  months (IQR 1.5-21.5) from device implantation to diagnosis. In all cases of palpitations symptoms with diagnosis AF with ventricular rapid response was found. For patients with syncope, atrioventricular conduction disturbance was demonstrated in 19.6%, sinus node dysfunction in 16.1%, paroxysmal supra-ventricular tachycardia in 7.1% and AF with slow ventricular rate in 1.8%. In the ischemic stroke case AF was detected after 5 months of monitoring (Table 3). There were no significant differences in the baseline ECG characteristics (rhythm disorders, intra-ventricular or atrioventricular conduction disturbance) or findings in the previous study, when compared to the group in which no diagnosis was obtained.

Subsequently to the diagnosis obtained by the ILR, the following therapeutic interventions were pursued: 19 patients received a permanent pacemaker, one a cardiac resynchronization therapy device, in five patients anticoagulation was introduced, and one was submitted to ablation of an accessory pathway.

There were no major complications reported during the implantation procedure or follow-up time. The mortality rate was 4.8% (n = 3) all from non-cardiac causes.

## Discussion

The objective of this study was to describe our center's experience with the use of ILR and establish its safety and efficacy in real world practice.

Current guidelines for the management of patients with syncope,<sup>2</sup> palpitations<sup>9</sup> and AF<sup>10</sup> recommend the use of prolonged electrocardiogram monitoring techniques to better establish a correlation between the symptoms and a specific ECG finding, so as to achieve a precise diagnosis. Its indication was also expanded to different clinical scenarios like the study of cryptogenic stroke or after myocardial infarction.<sup>3,11,12</sup> However, the 2014 European Heart Rhythm Association survey, which assessed the use of different monitoring techniques in the evaluation of patients with these clinical situations (unexplained syncope, palpitations and diagnosis

Table 1:

**Patient demographic and clinical characteristics. \* Left ventricular function quantification according to Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from American Society of Echocardiography and the European Association of Cardiovascular Imaging. Journal of the American Society of Echocardiography. January 2015**

Baseline characteristics	
Age (years old)	62.5 ± 18.8
Male gender	50.0 %
Hypertension	64.5%
Dyslipidemia	37.1%
Diabetes	16.1%
Ischemic heart disease	9.7%
Left ventricular function *	
Normal	88.7%
Mildly abnormal	3.2%
Moderately abnormal	6.5%
Severely abnormal	1.6%

Table 2:

**Electrocardiography characteristics. AV: atrioventricular; RBBB: right bundle branch block; LAFB: Left anterior fascicular block; LBBB: left bundle branch block**

ECG baseline characteristics	
Sinus Rhythm	95.2%
Atrial Fibrillation	4.8%
Normal QRS and AV conduction	63.1%
First degree AV block	12.5%
RBBB	4.9%
RBBB+ LAFB	8.0%
LAFB	1.6%
LAFB + First degree AV block	3.2%
LBBB	5.1%
LBBB + First degree AV block	1.6%

AF) in different European centers, found discrepancies and poor adherence to the guidelines regarding the use of IRL, specially in the management of patients with unexplained syncope, in which only a minority of non high-risk patients seemed to receive an IRL as part of their diagnostic practice.<sup>1</sup>

In our study, the main indication for ILR use was recurrent syncope/pre syncope (90.3%) and only a minority implanted ILR for palpitations complaints or in stroke investigation. This data demonstrate that clinicians are still reluctant to use ILR in situations like unexplained palpitations, cryptogenic stroke or AF. Moreover, in our study, IRL was only used after a previous extensive evaluation with several non-invasive and even invasive techniques, with 23.3% of the patients being submitted to more than two different types of complementary exams without a clear diagnosis before IRL implantation was considered. This approach is indubitably associated to higher costs and resources consumption, with longer period of time from symptoms to diagnosis. In the PICTURE registry that enrolled 570 patients, the median number of tests performed per patient was 13, being ECG, transthoracic echocardiogram, ambulatory ECG monitoring, in hospital ECG monitoring, exercise tests and orthostatic blood pressure measurement the tests most frequently performed.<sup>8</sup> The reason for this late referral to ILR implantation, shown in several studies and confirmed in our study, is unknown, especially after ILR had proven to be able to provide an earlier diagnosis of the underlying rhythm disturbance, along with a reduction in the number of advanced cardiac tests performed.<sup>8</sup> Recent studies showed that ILR monitoring is likely to be a cost effective strategy especially in patients who present infrequent symptoms suspected to be arrhythmic.<sup>13</sup>

In our study the diagnostic yield of the ILR was 46.8% over a period of  $12.8 \pm 14.4$  months and provided useful information in another 19.3% in which arrhythmic events were excluded as symptoms cause. These results are in accordance with other published data describing similar diagnostic rates.<sup>6,7,8</sup> Several randomized studies that compared the use of prolonged ILR monitoring to conventional tests in the study of unexplained syncope, demonstrated the efficacy and safety of the ILR as a diagnostic tool. The study of Krahn et al that included 60 consecutive patients with unexplained syncope randomized to IRL monitoring or conventional investigation, described a diagnostic yield of 52% vs 20% ( $p=0.012$ ).<sup>7</sup> The FRESH study presented a diagnostic rate of 46.2% with IRL monitoring for patients with unexplained syncope and the study of Farwell DJ. et al, a single center study that evaluated the diagnosis yield of IRL compared with conventional strategy showed that an ECG diagnosis was identified in 33% of ILR group in contrast with only 4% in the other patients.<sup>14,15</sup> Similar efficacy rates were also described for patients with palpitations. The RUP study, that included 50 patients with unexplained palpitation, compared the diagnostic rate and the costs of ILR implantation with the use of conventional strategy (24 hours Holter recording, a 4-week period of ambulatory ECG monitoring with an external recorder, and electrophysiological study). This study demonstrated the superiority of the IRL approach with a diagnosis rate of 73% vs 21% in conventional group ( $p<0.001$ ) and costs of  $3.056 \pm 363$  euro vs  $6.768 \pm 6.672$  euro ( $p=0.012$ ).<sup>16</sup>

The majority of our patients with episodes of syncope of arrhythmic origin had bradyarrhythmic events, with atrioventricular conduction disturbances or sinus node dysfunction as main causes. This data was in accordance with diagnostic findings in ISSUE study.<sup>2,17</sup>

**Table 3: Diagnostic findings according to ILR implantation reasons**

ILR implantation reason	Diagnostic finding	
Syncope (90.3%)	Atrioventricular conduction disturbance	19.6%
	Sinus node dysfunction	16.1%
	Paroxysmal supra-ventricular tachycardia	7.1%
	Atrial fibrillation	1.8%
Palpitations (8.1%)	Atrial fibrillation	100%
Ischemic stroke (1.6%)	Atrial fibrillation	100%

An interesting feature in our study was that all patients with palpitations complains in which a diagnosis was achieved had paroxysmal episodes of AF as cause of their symptoms. This is possibly explained by the paroxysmal nature of this arrhythmia, frequently presented by short but symptomatic episodes, most of which very difficult to diagnose with other monitoring methods. In RUP study the main diagnostic findings for palpitations symptoms were supraventricular tachycardia and AF/atrial flutter both in 6 of a total of 19 patients with a final arrhythmic diagnose.<sup>16</sup> Several data showed that AF detection increases with monitoring intensification. However the use of ILR in AF setting has some limitations especially related to their limited storage capacity and problems on the detection channel, with either undersensing or oversensing that can triggering storage of ECG data that have no clinical significance.<sup>18,19</sup>

The AF detection algorithm operates through an assessment on the regularity of RR intervals within a 2 minutes time window. It requires at least 2 minutes of AF for the device to recognize the rhythm as AF and automatically store the episode. Shorter episodes can only be captured manually activated by patients. Once AF is diagnosed, it is stored as a sustained AF episode within the automatic episode counter, showing date and time of occurrence as well as episode length. However, when storage is exhausted, older EGMs are overwritten with newer ones and only the final events are kept in the memory as EGM. Considering these limited storage capacity, the diagnostic accuracy of ILR may be lower in patients with a high number of false positive episodes.<sup>20,21</sup>

The initial study of Hindricks G. et al that access the performance of the ILR with a dedicated AF detection algorithm found a high sensitivity of 96.1% for AF detection and a high negative predictive value, while specificity was limited by falsely stored AF episodes in 15% of the patients.<sup>20</sup> Also in the study of Eitel C. et al, interrogations with automatically stored AF episodes containing only EGMs with sinus rhythm and artefacts leading to AF misdetection could be found in 22% in the group with conventional AF detection algorithm. The reasons found for AF misdetection were the occurrence of myopotentials/noise in 35%, T-wave oversensing in 1.5%, frequent premature ventricular or atrial complexes in 15% and R-wave undersensing in 4%.<sup>21</sup>

In order to supplant these limitations specific AF detection algorithms with a software upgrade have been developed. The mentioned upgraded software aims a reduction of noise induced false-positive AF episodes by reducing the noise rejection threshold from 60 to 5 seconds. Furthermore the patient can check whether EGM storage capacity is exhausted.<sup>21</sup>

The previous referred study of Eitel C. et al, had as main objective to analyse the performance of the implantable continuous AF detection device in a clinical setting before and after introduction of a software upgrade. The results demonstrated that the introduction of



the new software significantly reduced the number of patients with a misdetection of AF (72% vs 44%  $p=0.001$ ), mainly attributable to a significantly reduction of false AF detection due to myopotentials or noise. The number of patients with clinically non-diagnostic interrogations was also reduced from 38% to 16%.<sup>21</sup>

Additional to software developments, several other measures and follow-up strategies were proposed to increase the ILR accuracy: the need of confirmation on manual EGM analysis of all automatically detected episodes; prevention of EGM storage overcrowding with remote monitoring techniques, individual device programming and follow-up schedules or the presence of an alarm signal indicating full storage thus leading to a visit to the device clinic. Other possible measure could be prolongation of the detection period for sustained AF in order to prevent episodes of misdetection, but shorter AF episodes will then be unrecognized. However additional data are needed to assess the impact of these measures on ILR diagnostic accuracy in the clinical setting.<sup>18,19,21</sup>

Regarding the use of ILR on detection or in confirmation of absence of AF during long-term follow-up, especially after AF ablation procedures, ILR is also able to measure AF burden. In our study AF burden is not described, as data beyond the first detection of AF was not collected for study purpose. However, recent studies of pacemaker data have shown that morbidity is dependent on the burden of AF, supporting the value of its measurement.<sup>22</sup>

In our study, the baseline ECG characteristics or findings from previous exams were not predictive of diagnostic achievement in IRL. Predictive factors for ILR diagnosis have not been adequately investigated. In a recent study of Ahmed N et al. the authors studied predictors for pacemaker implantation in the IRL population with unexplained syncope. From a total of 200 patients with ILR for unexplained syncope, a pacemaker was implanted in 33 patients due to significant bradycardia. The predictive factors for occurrence of bradycardia necessitating pacemaker were predominantly clinical characteristics as history of injury secondary to syncope and female sex, with or without ECG conduction abnormalities.<sup>23</sup>

In the present study, no major adverse complications or events were reported during the implantation or follow-up period thus confirming the safety of this method.

The main limitations of our study were inherent to its design. It was a retrospective, observational, single-center study involving a small number of patients.

## Conclusions

In our experience, the ILR proved to be a safe and useful complementary diagnostic method, with a significant additional efficacy compared to other routine electrocardiographic monitoring methods. In our study, ILR has enabled the identification or exclusion of serious rhythm disturbances in more than half of patients and provided a targeted therapeutic intervention. These results are in accordance with published data and emphasize the early use of IRL in the investigation of symptoms with suspected arrhythmic basis.

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