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# Diagnostic value of implantable loop recorders in patients with unexplained syncope or palpitations

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## Abstract

**Background:** The implantable loop recorder (ILR) is a small cardiac rhythm-monitoring device. Our aim was to determine ILR diagnostic value in patients with unexplained syncope, presyncope, or palpitations suggesting cardiac arrhythmias.

**Methods:** This has been a retrospective, observational, single-center study. We included 181 patients in whom ILR was implanted at the Clinical Center of Serbia between January 2006 and July 2019. An event was marked as diagnostic if it led to a diagnosis and ILR was considered diagnostic if it verified or excluded an arrhythmia as the cause of syncope or palpitations.

**Results:** The mean age was 51.8 ± 17.8 years and 94 (51.9%) were male. The mean follow-up period was 20.2 ± 15.8 months. ILR was diagnostic in 98 patients (54.1%). There was no significant difference in diagnostic value of ILR in regard to the baseline patients' characteristics. The mean time to occurrence of the diagnostic event was 11.1 ± 9.6 months. The time to occurrence of a diagnostic event did not differ significantly between patients who underwent basic as compared to extended diagnostics before ILR implantation.

**Conclusions:** ILR was able to achieve an etiological diagnosis in 54.1% of patients with unexplained syncope, presyncope, or palpitations suggesting cardiac arrhythmias. In a subgroup of patients with recurrent palpitations, ILR was significantly less diagnostic than in patients with syncope or presyncope. ILR should be implanted beforehand in syncope evaluation process.

**KEYWORDS**
arrhythmia, implantable loop recorder, palpitations, syncope

Syncope is a transient, complete loss of consciousness due to transient global cerebral hypoperfusion, characterized by rapid onset, short duration, and complete spontaneous recovery (Ahmed et al., 2015; Moya et al., 2009; Shen et al., 2017). The etiology of syncope is difficult to determine due to its sporadic, infrequent, and unpredictable nature (Entem et al., 2009). Despite extended diagnostics, syncope remains unexplained in 17%–37% of patients (Vitale et al., 2010).

The implantable loop recorder (ILR) is a small implantable monitoring device that allows long-term electrocardiographic monitoring

(Entem et al., 2009; Kadmon et al., 2012). ILR has a battery life of up to 36 months, so the chance to record the direct correlation between the symptoms and the electrocardiogram is significantly higher than with the conventional diagnostic approach (Bovin et al., 2012; Moya et al., 2009). According to the latest guidelines, ILR implantation is indicated in the early assessment of recurrent unexplained syncope with suspected arrhythmic origin in non-high-risk patients, as well as in high-risk patients, but after comprehensive workup (Brignole et al., 2018; Moya et al., 2009; Shen et al., 2017).

Unexplained, recurrent palpitations are a less common indication for ILR implantation, mainly when suggesting cardiac arrhythmias in low-risk patients, and after complete pre-evaluation (Bisignani et al., 2019).

Our study aimed to assess a diagnostic value of ILR in evaluation of unexplained syncope, presyncope, or recurrent palpitations suggesting cardiac arrhythmias.

## 1 | METHODS

This has been a retrospective, observational, single-center study. The investigation conforms to the principles outlined in the Declaration of Helsinki. The study was approved by an institutional review committee.

### 1.1 | Study population

We included patients with unexplained syncope, presyncope, or recurrent palpitations suggesting cardiac arrhythmia. In all of them, ILR was implanted between January 2006 and July 2019 at the Pacemaker Center of the Clinical Center of Serbia. All patients, before ILR implantation, underwent a basic pre-evaluation (basic diagnostic workup) which included a careful medical history taking, physical examination, 12-lead electrocardiography (ECG), 24-h ambulatory ECG recording, and echocardiography. The extended diagnostic evaluation included head-up tilt-table test (HUTT) or carotid sinus massage or electrophysiological study and, when indicated, a neurological examination.

### 1.2 | Implantable loop recorder implantation

All patients gave informed consent for the implantation procedure. The ILR (Medtronic Reveal Plus, DX, XT or LINQ; St. Jude Medical (Abbott) Confirm; Biotronik BioMonitor) was positioned subcutaneously in the left pectoral region under local anesthesia with small incision or it was injected. ILR diagnostic parameters were programmed according to the manufacturers' recommendations and doctors' discretion. The automatic activation was programmed for a ventricular pause of >3 s, a ventricular rate of <40 beats/min, or a ventricular rate >180 beats/min for more than 16 beats. In addition, there was the possibility for the patient to activate the ILR by pressing a button in response to symptom occurrence (patient activation). Automatic algorithms for detection of atrial fibrillation were activated if available.

### 1.3 | Follow-up

During the follow-up period, in asymptomatic patients ILR was interrogated bimonthly, and in symptomatic patients on the first day after symptoms occurrence. The device remained implanted until a diagnostic event was recorded or until the end of a battery life, with a minimum follow-up of 12 months. An event was considered diagnostic if it led to the diagnosis. ILR was considered diagnostic if it helped verify or exclude arrhythmia as the cause of the syncope or palpitations. ILR was not considered diagnostic if it did not lead to the diagnosis at the time of explant or if the patient was still in follow-up. Safety of ILR implantation was assessed based on operative and postoperative complications. Data were collected from the medical records of ILR implantation and patients' files from device interrogations.

### 1.4 | Statistical analyses

For data processing, descriptive and analytic statistic methods were used. Data are presented as mean ± sd, or *n* (%) depending on data type. *t* Test and chi-square test were used to assess differences between examined groups. Log-rank test was used to test the difference between groups by occurrence of an event. All p values less than 0.05 were considered significant. All data were analyzed using SPSS 20.0 (IBM corp.) statistical software.

## 2 | RESULTS

### 2.1 | Study population characteristics

From January 2006 to July 2019, 204 ILR devices were implanted at the Pacemaker Center of the Clinical Center of Serbia. Ten patients were lost to follow-up; in 13 patients, ILR was implanted in the indication of cryptogenic stroke. Therefore, 181 patients were included in the study. During follow-up, 13 months after ILR implantation, one patient died. It was a young person with a complex congenital heart defect, who died in the worsening of advanced pulmonary hypertension, without arrhythmic events during follow-up. The mean age of the study population was 51.8 ± 17.8 years and 94 (51.9%) were male. In the study population, the most common indication for ILR implantation was recurrent syncope, in 122 patients (67.4%), followed by single syncope in 24 patients (13.3%), presyncope in 19 (10.5%), and palpitations suggesting arrhythmia 16 patients (8.8%). Patients' clinical characteristics are presented in Table 1. The basic pre-evaluation diagnostic workup was performed in all patients before ILR implantation. The extended diagnostics was completed in

60 patients (33.1%), including a carotid sinus massage (23 patients), head-up tilt test (42 patients), and electrophysiological examination (13 patients). The neurological examination and/or color Doppler ultrasound of carotid arteries were performed in 137 patients (75.7%) before intervention. One hundred and twenty-four (68.5%) patients were using the cardiovascular drugs in chronic therapy, mostly ACE inhibitors/angiotensin II receptor blockers (48.6%), beta blockers (38.7%), other antiarrhythmics (11.6%), Ca channel blockers (17.1%), diuretics (16.6%), mostly thiazide diuretics (13.8%), statins (27.1%), acetylsalicylic acid (29.8%), and oral anticoagulants (13.3%). The mean left ventricular ejection fraction in the whole study population was 60.2 ± 7.5%, within the group of patients with structural heart disease 54.8 ± 10.7% and without 61.3 ± 6.1% ($p < .01$). The mean follow-up period was 20.2 ± 15.8 months.

**TABLE 1** Clinical characteristics of patients

| Parameter | Number of patients (%) |
|---|---|
| Age | 51.8 ± 17.8 |
| Sex (male) | 94 (51.9%) |
| Structural heart disease | 32 (17.7) |
| Ischemic heart disease | 18 (9.9) |
| Dilated cardiomyopathy | 6 (3.3) |
| Hypertrophic cardiomyopathy | 2 (1.1) |
| Heart valve disease | 5 (2.8) |
| Congenital heart disease | 1 (0.6) |
| Atrial fibrillation before implantation | 30 (16.6) |
| Paroxysmal atrial fibrillation | 26 (14.4) |
| Permanent atrial fibrillation | 4 (2.2) |
| Bundle branch block | 15 (8.3) |
| Left bundle branch block | 7 (3.9) |
| Right bundle branch block | 8 (4.4) |
| Chronic obstructive pulmonary disease | 9 (5.0) |
| Arterial hypertension | 95 (52.5) |
| Diabetes | 14 (7.7) |
| Hyperlipidemia | 45 (24.9) |
| Tobacco smoking | 49 (27.1) |
| Cardiovascular heredity | 24 (13.3) |

## 2.2 | Diagnostic value of ILR

ILR was diagnostic in 98 patients (54.1%), in 80 patients (81.6%) the cause of syncope or palpitations was arrhythmic, and in 18 patients (18.4%) arrhythmia was precluded as the cause of symptoms (Table 2). Dual-chamber pacemakers were implanted in all but one patient (14 patients) with AV block 2nd or 3rd degree. Of 45 patients with diagnosed sinus node dysfunction, 38 underwent implantation of pacemaker in DDDR, 4 in VVIR, 1 in AAIR mode of stimulation, and two patients refused the intervention, despite the obvious indication. In two patients with atrial fibrillation, slow ventricular rate and pause longer than 3s VVIR pacemakers were implanted. In two patients, AV node re-entry tachycardia was recorded, in three patients supraventricular tachycardia and frequent premature ventricular contractions correlated with symptoms in one patient, and they all underwent successful radiofrequency ablation. In one patient with supraventricular tachycardia and two with ventricular extrasystoles, an antiarrhythmic therapy was administered. Atrial fibrillation with fast ventricular rate was registered in three patients, in two with paroxysmal form it was resolved by pulmonary vein isolation, while in one patient with permanent form it was solved by AV node ablation and CRT-ICD implantation. ICD-VR was implanted in four patients and ICD-DR in two patients with sustained ventricular tachycardia. Of 16 patients with recurrent palpitations, ILR was diagnostic in four—in two patients, supraventricular tachycardia was diagnosed, one had paroxysmal atrial fibrillation, and the remaining patient had sustained ventricular tachycardia.

In 18 patients, ILR was considered diagnostic since it enabled the exclusion of arrhythmia as the cause of the syncope or palpitations. Among them, epilepsy was the final diagnosis in 8 patients,

**TABLE 2** Established diagnosis and treatment measures in patients with implantable loop recorder -guided diagnosis of arrhythmic syncope or palpitations

| Diagnosis | Number of patients (%) | Therapy | | |
|---|---|---|---|---|
| | | Pacemaker therapy | Ablation | Medical therapy |
| Atrial fibrillation—bradyarrhythmia | 2 (2.5) | 2 | 0 | 0 |
| Sinus node dysfunction | 45 (56.3) | 43* | 0 | 0 |
| AV block 2nd and 3rd degree | 15 (18.7) | 15 | 0 | 0 |
| Supraventricular tachycardia | 4 (5) | 0 | 3 | 1 |
| AV node re-entry tachycardia | 2 (2.5) | 0 | 2 | 0 |
| Ventricular premature complexes that correlate with symptoms | 3 (3.7) | 0 | 1 | 2 |
| Ventricular tachycardia | 6 (7.6) | 6 | 0 | 0 |
| Atrial fibrillation—tachyarrhythmia | 3 (3.7) | 1 | 2 | 0 |
| Total | 80 (100) | 67 | 7 | 4 |

*Two patients refused pacemaker implantation.

psychogenic non-epileptic seizures in two, non-cardiac syncope in two, and in 6 patients, further neurological monitoring and close follow-up were indicated.

ILR was not diagnostic in 83 patients (45.9%). Seventy-six patients were asymptomatic and 7 had symptoms that did not meet our criteria for a diagnostic event, so it was decided not to explant the device and continue monitoring (hemorrhoidal bleeding followed by syncope was noticed in one patient, another had fainting during a strong cough, a third had the same symptom during a sudden getting out of bed, and the remaining four patients experienced dizziness during follow-up). In 51 patients, ILR was explanted due to the end of a battery life, while 32 patients are still being followed up.

The mean time to the occurrence of a diagnostic event was 11.1 ± 9.6 months. The mean time from ILR implantation to device explant was 13.1 ± 12.2 months in patients with diagnostic ILR and 18.1 ± 15.3 months in the entire study population. There was no significant difference in diagnostic value of ILR in regard to the baseline patients' characteristics, except for recurrent palpitations as an indication for ILR implantation (Table 3). Time to the occurrence of a diagnostic event was not significantly different between patients who underwent basic as compared to extended diagnostics before ILR implantation, ($p$ = .402, Figure 1). The diagnostic value of ILR did not differ significantly between groups of patients with basic versus extended diagnostics ($p$ = .871), although mean age, incidence of atrial fibrillation, and structural heart disease before ILR implantation were different between these two groups of patients (Table 4).

### 2.3 | Safety of ILR implantation

There were 3 (2.9%) complications related to the implant, one hemostasis revision, one device reposition due to unsatisfactory ECG, and one local pocket infection 3 months after the implantation, resolved by device explantation and antibiotics administration.

## 3 | DISCUSSION

The role of ILR in determining the etiology of recurrent syncope changed significantly over time. Primarily, ILR was indicated in patients with recurrent, highly likely arrhythmic syncope, but with unclear underlying mechanism after complete diagnostic evaluation (Brignole et al., 2004). Over time, studies have shown that prolonged monitoring is comparable to the conventional diagnostic approach, and a more cost-effective strategy, capable to get a diagnosis faster and more often (Kang et al., 2013; Krahn et al., 2003). According to the latest guidelines, ILR is indicated in an early phase of evaluation in patients with recurrent syncope of uncertain origin, the absence of high-risk criteria, and high likelihood of recurrence within battery longevity of the device and after a comprehensive workup in high-risk patients (with severe structural or coronary artery disease) (Brignole et al., 2018; Moya et al.,l., 2009). It is estimated that two-thirds of patients with unexplained syncope have indications potentially appropriate for ILRs (Vitale et al., 2010). However, there is a discrepancy between clinical practice and the indications provided by the guidelines, with estimated indications four times higher than those achieved (Ahmed et al., 2015; Vitale et al., 2010). In patients with palpitations not followed by syncope, the guidelines for ILR implantation are not strict, and when we assume that cardiac arrhythmia is the cause of the symptoms, ILR implantation may be indicated (Bisignani et al., 2019; Giada et al., 2007).

### 3.1 | General diagnostic value of ILR

In this study, ILR was diagnostic in 54.1% of patients. In 81.6% of them, the cause of syncope or palpitations was arrhythmic. Published studies have shown a broad diagnostic yield ranging from 22 to 73% depending on the primary indication of ILR (Sakhi et al., 2018). In PICTURE study, the largest prospective, multicenter study, during the average follow-up period of 10 ± 6 months, 38% of included patients had syncope, in 78% of them ILR-guided diagnosis was obtained, and 75% had cardiac syncope (Edvardsson et al., 2011). In a large meta-analysis by Solbiati et al., diagnostic yield of ILR was 44%, but only about one half of patients finally diagnosed by an ILR had an arrhythmic syncope (Solbiati et al., 2017). In a study of Lee et al., which is comparable to ours, ILR detected arrhythmia in 57.2% of patients and syncope-correlated arrhythmia was confirmed in 19.7% of patients (Lee et al., 2020).

Comparing to the results of other authors, in our study fewer patients had symptomatic episodes with no arrhythmic abnormalities

**TABLE 3** Dependence of the diagnostic value of implantable loop recorder on patients' baseline clinical characteristics or associated diseases

| Parameter | Number of patients | Diagnostic ILR | $p$ value |
|---|---|---|---|
| Atrial fibrillation before implantation | 30 | 21 | .056 |
| Recurrent syncope as an indication for ILR implantation | 122 | 69 | .349 |
| Recurrent palpitations as an indication for ILR implantation | 16 | 4 | .014 |
| Bundle branch block | 15 | 8 | .948 |
| Arterial hypertension and/or diabetes | 97 | 58 | .101 |
| Structural heart disease | 32 | 16 | .604 |
| Ejection fraction ≤50% | 25 | 13 | .817 |

detected by ILR (Huemer et al., 2019; Kabra et al., 2009). In such cases, the role of ILR is to exclude arrhythmia as primary cause of syncope or palpitations, and the final diagnosis is usually made by a neurologist (in our study, eight patients had unrecognized epilepsy, two psychogenic non-epileptic seizures, and in six, prolonged neurological monitoring was indicated). Vice versa, it was reported that 30%–42% of patients initially diagnosed with epilepsy actually had syncope with convulsive activity due to cardiovascular etiology, although a cardiac event does not necessarily exclude a diagnosis of epilepsy (Kanjwal et al., 2009). In the remaining seven symptomatic patients, it was not possible to set the definitive diagnosis; therefore, ILR was not considered diagnostic, but it was decided to continue monitoring (it is our belief that ILR should remain implanted until the end of a battery life). Some studies showed that in one-quarter of patients symptoms occurred after more than 18 months of monitoring (Furukawa et al., 2012). In our study, the mean time to occurrence of a diagnostic event was about 11 months, and in about 20% of patients, it occurred after more than 18 months of follow-up.

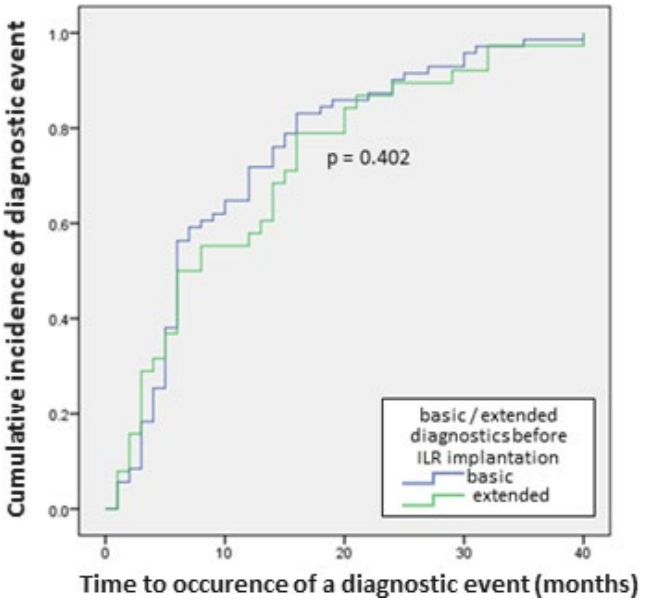


**FIGURE 1** The Kaplan-Meier estimates of time to diagnostic event in patients who underwent basic vs. extended diagnostics before implantable loop recorder implantation

## 3.2 | ILR diagnostic value in different subpopulations

Our findings suggest that ILR should be implanted in all patients with an indication according to the latest guidelines, regardless of whether structural heart disease or bundle branch block is present or not. Lacunza-Ruiz et al. also concluded that patients with structural heart disease or bundle branch block had a similar rate of diagnoses obtained by ILR and the type of diagnosis provided by the device (Lacunza-Ruiz et al., 2013). Sakhi et al. found a similar diagnostic value of ILR in patients with and without structural heart disease, but they emphasized the difference in the arrhythmia mechanism in these two groups, indicating a higher incidence of nonsustained VT in patients with structural heart disease as well as more frequent ICD implantation in this group of patients (Sakhi et al., 2018). On the other hand, one should be more careful in indicating the ILR implantation in patients with recurrent palpitations suspected to be caused by arrhythmia, but not followed by syncope. It has been shown that in this indication, although symptoms indicate the presence of a cardiac arrhythmia, ILR is statistically significantly less diagnostic.

Also, our results confirmed that extended diagnostics does not increase the diagnostic value of ILR, or shorten the time to final diagnosis, while enhancing health care-related costs (Giada et al., 2007). In PICTURE study, it was calculated that the median number of tests performed per patient in the total study population was 13 (Edvardsson et al., 2011). The early use of ILR will reduce the number

**TABLE 4** Characteristics of patients with basic and extended diagnostics before implantable loop recorder implantation

| Parameter | Study population | Group with only basic diagnostics | Group with extended diagnostics | *p* value |
|---|---|---|---|---|
| Patients | 181 (100%) | 121 (66.8%) | 60 (33.2%) | |
| Age | 51.8 ± 17.8 | 54.4 ± 17.3 | 46.5 ± 17.7 | .004 |
| Sex (male) | 94 (51.9%) | 61 (50.4%) | 33 (55.0%) | .561 |
| Hypertension | 95 (52.5) | 69 (57.0%) | 26 (43.3%) | .082 |
| Diabetes | 14 (7.7) | 9 (7.4%) | 5 (8.3%) | .832 |
| Hyperlipidemia | 45 (24.9) | 31 (25.6%) | 14 (23.3%) | .738 |
| Chronic obstructive pulmonary disease | 9 (5.0) | 7 (5.9%) | 2 (3.3%) | .475 |
| Tobacco smoking | 49 (27.1) | 31 (25.6%) | 18 (30.0%) | .532 |
| Atrial fibrillation | 30 (16.6) | 28 (23.1%) | 2 (3.3%) | <.01 |
| Block bundle branch | 15 (8.3) | 12 (9.9%) | 3 (5.0%) | .259 |
| Structural heart disease | 32 (17.7) | 27 (22.3%) | 5 (8.3%) | .02 |
| Diagnostic ILR | 98 (54.1%) | 65 (53.7%) | 33 (55.0%) | .871 |

of cardiology tests, and thus, the burden on the healthcare system (Podoleanu et al., 2014). Cost–benefit analyses comparing ILR and conventional diagnostic workup showed higher overall mean costs in the ILR group, when the ILR cost is counted, but, on the other hand, the mean cost per diagnosis and the mean cost per arrhythmic diagnosis were lower for participants randomized to the ILR group (Solbiati et al., 2016).

Recently, the indications for ILR implantation have expanded, like in patients with recurrent vasovagal syncope, in patients with cryptogenic stroke in order to detect silent atrial fibrillation, or to establish medical or device therapy based on risk stratification in patients with inherited cardiomyopathies, or after myocardial infarction or after the episode of acute heart failure (Bisignani et al., 2019; Brignole et al., 2014; Lacunza-Ruiz et al., 2013).

Finally, our results showed that ILR implantation is a safe procedure, which is not related to major complications.

Our findings indicate that etiological diagnosis of unexplained syncope can be achieved in more than half of patients after ILR implantation. When implanted in patients with recurrent, undocumented palpitations, ILR is significantly less often diagnostic. There is no specific group of patients that benefits more, given that syncope management using ILR seems to be independent of concomitant findings and comorbidities. In accordance with current guidelines, ILR should be implanted beforehand in syncope evaluation process, since extended diagnostics does not increase the diagnostic value of ILR, or shorten the time to final diagnosis.

## CONFLICT OF INTEREST

None.

## ETHICAL APPROVAL

This study was approved by the local institutional ethics committee.

## 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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