A Review of the Wide Range of Indications and Uses of Implantable Loop Recorders: A Review of the Literature

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Abstract: Implantable loop recorders (ILR) are devices that are implanted subcutaneously on the chest, which enables the continuous monitoring of arrhythmias for up to three years. These devices have an important role in helping to make a diagnosis and supporting decisions about the best patient management. There are currently three companies that produce ILRs. The Reveal DX and XT device is produced by Medtronic. The Confirm device is produced by Abbott. The Biomonitor III device is produced by Biotronik. The established indications for ILR include the management of transient loss of consciousness and the diagnosis of undocumented palpitations; however, they are also used for less established applications, including atrial fibrillation (AF) monitoring and risk stratification in patients with previous myocardial infarction or inherited cardiomyopathies. There is also diverse literature exploring the use of these devices in other populations, including patients with conditions such as congenital heart disease, amyloidosis, stroke, obstructive sleep apnea, renal transplant and patients who undergo procedures such as AF ablation and coronary artery bypass graft. In this review, we describe how the use of ILR has been applied in different settings, including patients with cardiac and non-cardiac conditions as well as post-cardiac procedures. We then discuss the potential issues related to using ILR in these other indications.

Keywords: implantable loop recorder; arrhythmia; atrial fibrillation

1. Introduction

Implantable loop recorders (ILR) are devices that are implanted subcutaneously on the chest, which enables continuous monitoring of arrhythmias for up to three to five years. They have an important role in the care of patients with suspected or underlying cardiac arrhythmia as they enable the capturing of cardiac electric activity during symptomatic episodes and the detection of asymptomatic arrhythmic events. These devices are easily implanted as they are a less-than-20-min procedure under local anaesthetic. They have an important role in making a diagnosis and in supporting decisions about patient management. While continuous monitoring of electrical activity can take place in a hospital via telemetry, these devices have the advantage that monitoring can take place when patients are in the community and doing everyday activities. They overcome the limitation of cardiac tape recorders, which monitor for shorter periods of time (e.g., 24 h, 48 h, 7 days), during which time the arrhythmia may not occur. Furthermore, ILR does not require patient activations to commence monitoring, which can be helpful in patients who become quickly incapacitated when arrhythmias occur. They can also be used to help provide reassurance to patients. However, in addition to the cost of implanting the device and services to monitor for arrhythmias, the ILR does have limitations as it requires an invasive procedure to implant and is associated with a small risk of pain, bleeding, infection and

detection of false-positive arrhythmias. The device is small such that patients may initially notice there is something under the skin, but it does not normally interfere in any way with any physical activity.

There are currently a few ILRs available on the market. The Reveal DX and XT device is produced by Medtronic. The Confirm is produced by Abbott. The Biomonitor III is produced by Biotronik. They are currently used as a monitoring device for patients with recurrent unexplained episodes of palpitations or syncope or for long-term monitoring of patients at risk or having known arrhythmias. The established indications for ILR include management of transient loss of consciousness and diagnosis of undocumented palpitations; however, there are fewer established applications, including atrial fibrillation (AF) monitoring and risk stratification, in patients with previous myocardial infarction or inherited cardiomyopathies [1]. However, there is diverse literature exploring the use of these devices in other populations, including patients with conditions such as congenital heart disease, amyloidosis, stroke, obstructive sleep apnea, renal transplant and also patients who undergo procedures such as AF ablation and coronary artery bypass graft.

In this review, we describe some of the less established applications of ILR in different patient populations. We then discuss the potential issues related to using ILR in these other indications.

2. Application of ILR in Cardiac Conditions

2.1. Heart Failure and Post-Myocardial Infarction

Heart failure is a condition that places patients at risk of arrhythmias which can exacerbate symptoms and result in arrhythmic complications such as systemic or cerebral embolism with atrial flutter or fibrillation or cardiac arrest with ventricular arrhythmias [2]. Kort et al., evaluated 30 patients with heart failure from three Dutch teaching hospitals who underwent ILR implantation [3]. Over a median follow up period of 12 months, 12 patients with heart failure with reduced ejection fraction and three patients with heart failure with preserved ejection fraction had arrhythmias. The arrhythmias detected included bradycardias, non-sustained ventricular tachycardia, asystole, AF, atrioventricular block and supraventricular tachycardia. Only one patient with atrioventricular block had a pacemaker implanted, and many patients had medication changes, including initiation of oral anticoagulation for AF and β-blocker dose alteration. While 20 patients had AF detected on ILR, 12 were considered false positives after expert adjudication. A few trials have examined the use of ILR to detect arrhythmias in patients with heart failure post-acute myocardial infarction. The CARISMA study evaluated 297 patients with acute myocardial infarction who had left ventricular ejection fraction ≤40% and an implantable cardiac monitor who were followed up for an average of 1.9 years and found that bradyarrhythmias and tachyarrhythmias were recorded in 46% of patients which included new-onset atrial fibrillation, non-sustained ventricular tachycardia, high-degree atrioventricular block, sinus bradycardia, sinus arrest, ventricular tachycardia and ventricular fibrillation [4]. Detection of these arrhythmias, particularly high-degree atrioventricular block, was important as it was associated with a more than six-fold risk of death [4]. However, the clinical utility of loop recorders remains questionable as implanting the loop recorder did not have an impact on subsequent mortality, but it may have value in the evaluation of symptoms possibly related to arrhythmias [5]. The more recent SMART-MI trial randomised survivors of acute myocardial infarction in sinus rhythm and a left ventricular ejection fraction of 35–50% with autonomic dysfunction to an ILR or conventional follow up [6]. This trial of 400 patients found that serious arrhythmic events were detected in 30% of patients in the ILR group compared to 6% of patients in the control group, and the trial concluded that telemonitoring with ILR was highly effective in early detection of subclinical, prognostically relevant arrhythmic events [7]. The main limitation of the trial was that it was a diagnostic trial, and no conclusion can be drawn with regard to the effect of monitoring on therapies and related outcomes. These trials suggest that there may be a role for patients to have ILR

post-myocardial infarction, particularly those who may have symptoms of arrhythmia or are at high risk of arrhythmias, but more studies are needed.

2.2. Adult Congenital Heart Disease

Rhythm disorders are a major cause of morbidity, mortality and poor quality of life in patients with adults with congenital heart disease [8]. The entire spectrum of arrhythmias can be encountered in adults with congenital heart disease, and some may relate to the underlying malformation itself, while others may be related to the type and timing of adult congenital heart disease repair [9]. Patients with congenital heart disease who develop AF have a poor prognosis, and detection of AF may indicate deterioration in their condition and may warrant early investigation. Dodeja et al., carried out a retrospective review of 22 patients with adult congenital heart disease who underwent ILR. In this group, 32% had Fontan palliation, 32% had Tetralogy of Fallot, and the remaining patients had pulmonary stenosis, transposition of the great arteries, Ebstein's anomaly, bicuspid aortic valve, interrupted aortic arch, coarctation and congenital aortic stenosis. Dodeja et al., found that nine (41%) of patients had a change in their clinical management because of ILR findings and that three patients were asymptomatic. The changes in management included medication alterations and pacemaker insertion for patients with pauses, electrophysiology study for supraventricular tachycardia, anticoagulation for AF, cardioversion and amiodarone for atrial flutter and sotalol and implantable cardioverter defibrillator for ventricular arrhythmias. Patients with Fontan palliation had the highest percentage of pertinent positive events (57%), and 75% of patients with positive events had arrhythmias that were not previously detected on previous Holter/event monitors.

2.3. Cardiac Light Chain Amyloidosis

Patients with amyloidosis are at risk of conduction disease, including significant bradyarrhythmias, which may be amenable to device intervention. In young patients where bradyarrhythmias are detected, there is an important role in investigating amyloidosis as there are now important treatments. Arrhythmias are common in people with cardiac amyloidosis with conduction defects and atrial arrhythmias being more prevalent in transthyretin amyloidosis compared with people with light chain amyloidosis [10]. Sayed et al., conducted an evaluation of 20 patients with newly diagnosed severe cardiac light chain (AL) amyloidosis and symptoms of syncope or pre-syncope [11]. After following up with the patients for a median of 308 days, they found that 13 patients died, with a median survival of 61 days from device insertion. In eight patients, death was heralded by bradycardia, usually associated with complete atrioventricular block, followed by pulseless electrical activity, and four patients received pacemakers for a complete atrioventricular block, of which three later died. None of the symptom-driven downloads showed any rhythm change from baseline, and there was no association between timing and dosage of chemotherapy and changes in cardiac rhythm.

2.4. Postural Orthostatic Tachycardia Syndrome

Postural orthostatic tachycardia syndrome (POTS) is defined as a clinical syndrome of frequent symptoms such as lightheadedness, palpitations, tremulousness, generalised weakness, blurred vision, exercise intolerance and fatigue with an increase in heart rate of ≥ 30 bpm or a heart rate ≥ 120 bpm within the first 10 min of assuming an upright posture or during a head-up tilt test [10,12]. Syncope in POTS has been described to be due to a late phase surge in parasympathetic tone or sympathetic withdrawal leading to cardioinhibition and vasodepression [13,14]. In order to understand the cardiac electrical activity in patients with POTS, Kanjwal et al., evaluated 39 patients with POTS who had recurrent syncope despite medical therapy and an inconclusive Holter and event monitor. In this cohort, 27 patients had prolonged asystole (>6 s) or severe bradycardia (heart rate <30 bpm) during their syncope. A subset of 15 patients had asystole of >10 s with prolonged convulsive syncope without any warning. All patients underwent pacemaker

implantation, and syncope was eliminated, but patients continued to have orthostatic tachycardia and dizziness.

3. Application of ILR in Non-Cardiac Conditions

3.1. Cryptogenic Stroke

There is a strong association between AF and stroke [15]. Routine methods of AF detection post-acute stroke include a 12-lead resting electrocardiogram (ECG), additional ECG monitoring while in hospital and Holter monitoring after discharge at any time point. Detection of AF after acute stroke has been reported to be 1.7–16% on resting 12-lead ECG, 0.2–13% for the first 24 h after acute stroke from continuous monitoring, 2.3–11% for the first 72 h and 1.7–14% within a week after stroke [16]. The use of ILR in stroke patients provides an additional means to detect AF as the potential underlying cause of cryptogenic stroke, which has been evaluated in many studies. In the study by Carrazco et al., 31 out of 100 patients with cryptogenic stroke had paroxysmal AF detected on ILR, and obesity was the only factor in multivariate regression that was significantly associated with paroxysmal AF [17]. Results from the SURPRISE study suggest that 18 (20.7%) of 85 patients with cryptogenic stroke had asymptomatic paroxysmal AF over a mean follow up of 569 days, with the first event of paroxysmal AF occurring at a mean of 109 days [18]. Cotter et al., evaluated 51 patients with unexplained ischemic stroke and found that 25.5% had AF and that AF was associated with increasing age, interatrial conduction block, left atrial volume, and atrial premature contractions on previous monitoring [19]. Israel et al., evaluated 123 patients with embolic stroke of undetermined source and found that 23.6% had AF during a mean follow up of 12.7 months, and patients who had AF were older, with higher CHA2DS2-VASc scores and more often cerebral microangiopathy [20]. The most high profile study, CRYSTAL-AF, randomised 441 patients with insertable cardiac monitor versus conventional follow-up and found that at 6 months, AF was detected in 8.9% of patients with cardiac monitor compared to 1.4% of patients with conventional treatment, and at 12 months, this increased to 12.4% compared to 2.0% [21]. Collectively these findings make it clear that there is a major role for ILR in patients with cryptogenic stroke.

3.2. Elderly Patients with Risk Factors for Stroke

The recent LOOP study randomised patients aged 70 to 90 years with at least one risk factor for stroke to ILR monitoring or usual care [22]. This study of 6004 patients, of which 25.0% received ILR and 75% had usual care found that over a median follow up of 64.5 months, 1027 patients developed AF, which was 31.8% in the ILR group and 12.2% in the usual care group. While there was a three-fold increase in AF detection, there was no significant reduction in the risk of stroke or systemic arterial embolism (HR 0.80 95%CI 0.61–1.05, $p = 0.11$). A key consideration with AF detection is what duration that translates to an increased risk of stroke that anticoagulation can have an effect on. Use of 6 min duration as the cutoff for anticoagulation resulted in greater bleeding than stroke prevention (HR 1.26 95%CI 0.95–1.69, $p = 0.11$) when perhaps AF duration of >24 h may convey increased risk of stroke in relation to bleeding risk.

3.3. Obstructive Sleep Apnea

AF is strongly associated with obstructive sleep apnea [23]. The REVEAL XT-SA study by Yeung et al., evaluated the occurrence of newly detected AF in patients with severe obstructive sleep apnea with no previous history of AF [24]. A total of 25 patients were included, and 5 (20%) had ≥10 s of AF over the mean follow up of 27 months. The mean time to diagnosis was 11 months, and the male gender was the only predictor of AF detection ($p = 0.04$). In terms of safety, one patient had ILR reimplant due to a minor pocket infection, while two patients withdrew due to silicon allergy and pain.

4. Application of ILR in Monitoring Therapies

4.1. AF Ablation

The primary aim of AF ablation is to eliminate the symptoms associated with AF. The implantation of an ILR is therefore useful to monitor patients post-procedure for AF recurrence as well as documentation of what any recurrent symptoms may be due to. Bjorkenheim et al., evaluated 57 patients who underwent AF ablation following ILR implantation [25]. After two years of follow up, only 13 (24%) of patients had no AF episodes, and among patients with AF recurrence, 10 (24%) of the 41 patients only had AF recurrences detected by ILR. The burden of AF detected after ablation was low at a median of 5.7% over the 24 months follow up period, which supports continuous monitoring over intermittent follow up for detection of AF recurrence. Symptom activations were also frequently not associated with AF-out of 341 symptomatic episodes in 26 patients, only 228 (67%) correlated with AF. Forkmann et al., evaluated 126 patients with paroxysmal or persistent AF who underwent AF ablation and loop recorder. They found that within the 3 month blanking period, 57% of patients experience AF/atrial tachycardia recurrence and that there was a significant correlation between AF at this time and later recurrence at 12 months [26]. In general, AF ablation shows overall freedom from recurrence at 1 year in the range of 75% and that ongoing palpitations post-AF ablation may be due to AF but also atrial tachyarrhythmias and atrial ectopics where continuous monitoring has value due to the non-sustained nature of these arrhythmias.

4.2. Coronary Artery Bypass Graft

AF has been reported to occur in 18.5% to 33% of patients who undergo coronary artery bypass grafting [27,28]. El-Chami et al., evaluated 23 patients undergoing CABG with perioperative AF and an increased risk of stroke characterised by a CHADS2 score of ≥2 in the MONITOR-AF study [29]. During the 25-month follow-up period, 60.9% of patients experienced recurrent AF and the average time to the first occurrence of AF was 146 days. In addition, only one out of 14 patients were symptomatic, while the rest of the patients had AF diagnosed on ILR routine transmissions. No clinical or demographic risk factor predicted early vs late AF recurrence, and two patients required pacemaker insertion because of symptomatic sinus pauses.

5. Discussion

Our review demonstrates that there is literature that ILR has potential diagnostic value in patients with cardiac and non-cardiac conditions as well as those who undergo procedures that place patients at risk of arrhythmias. For some conditions, it is apparent that detection of arrhythmia can be of value as secondary prevention of events such as anticoagulation in cryptogenic stroke or identification of AF in obstructive sleep apnea. These findings suggest that in any patient population where there is a need to reliably detect arrhythmias, ILR should be considered, especially when there are negative random ECG and Holter monitoring.

An important consideration is that the benefits of implanting an ILR outweigh the risks. The rhythm monitoring of ILR is important, but also the actions are taken once abnormal heart rhythms are detected. Future work must consider the cost-benefit analysis in order to verify the cost associated with ILR implant and any automatic arrhythmia detected do translate into improved patient outcomes, as there may be the potential for false-positive findings. In addition to the physical implantation of the device, there are resources needed to manually check all the alerts. There is also the additional consideration, albeit small, of the risk of infection.

Syncopal events are common, as 19% of the United States population will experience an event in their lifetime, and 3% of emergency department visits and up to 6% of admission to hospitals are for syncope [30]. Therefore in a healthcare system where services are not paid for, it would not be financially possible to implant these devices in all patients who may meet the criteria of unexplained syncope. There should nevertheless have this option

of device available for patients who have infrequent symptoms which may be suspected of arrhythmia.

A few considerations should be made about the cardiac conditions highlighted in this review. In adult congenital heart disease, it is clear that these patients are at high risk of developing arrhythmias, and there may be diagnostic value in the use of an ILR device. However, it is important to recognise that there may be less expensive measures that can capture the arrhythmia. One approach may be that if patients have the random ECG and Holter/event monitoring and they all come back normal, they should be considered for patient monitors such as AliveCor/Apple watch or have an ILR device. The other important consideration is the estimated risk of arrhythmia based on the history and the underlying congenital heart diseases, which may help determine which patients would most benefit from ILR implantation. A key issue regarding the value of ILR is when it should be implanted for a condition as it should be before it is too late in the disease course. It may be that patients with mild disease who are symptomatic may benefit from the detection of arrhythmia rather than those with severe diseases which carries a poor prognosis. Heart failure is a non-specific syndrome that can be caused by ischemia but also inherited or acquired cardiomyopathy. The propensity to develop arrhythmias in heart failures depends on the underlying aetiology; some of these patients who are at high risk of arrhythmias should have an ILR device.

For non-cardiac conditions, the strong association between ischemic stroke and AF makes it important to identify from a diagnostic and management perspective. Detection of AF after acute stroke is suboptimal, and the use of ILR can greatly improve AF identification and support the use of anticoagulation for secondary prevention. While the association between AF and obstructive sleep apnea is also well described, it is not clear whether all or some patients with AF should have a loop recorder, especially in patients who do not have palpitations, syncope or stroke. Furthermore, the physiological changes in severe or end-stage chronic kidney disease make patients at risk of arrhythmias and patients may benefit from ILR implantation to identify arrhythmias. However, it should be that the patients should stand to benefit from arrhythmia detection and that less costly methods such as random ECG and Holter monitoring are unable to detect the arrhythmia. In addition, there are other non-invasive monitors currently available such as Apple watches and AliveCor devices, and the role of ILR may be more for asymptomatic episodes where there may be difficulties using these other non-invasive methods.

ILR device transforms the reliability of detecting arrhythmia in patients, and this can have clinical and research implications. The approach of using the ILR to detect arrhythmia is a more robust method than relying on patient symptoms, intermittent ambulatory ECG or Holter/event monitor evaluation. This may have a key role post procedures which are intended to treat arrhythmias such as AF ablation. In research settings, this has been used to compare the efficacy of different ablation techniques. For example, Adiyaman et al., conducted a trial of patients with symptomatic paroxysmal or early persistent AF who underwent catheter or surgical ablation and found that percutaneous pulmonary vein isolation was non-inferior to minimally invasive thoracoscopic pulmonary vein isolation with left atrial appendage ligation [31]. A similar approach of using ILR was used for the randomised study of catheter ablation and convergent epicardial and endocardial ablation procedure [32]. There is also the potential role of ILR in studies to predict arrhythmias. For example, ILR has been used in a general population who underwent cardiac magnetic resonance imaging in order to show that extent of left atrial fibrosis as measured by left atrial late gadolinium enhancement was associated with incident AF detected on loop recorder [33].

An important consideration is the accuracy of ILR in identifying arrhythmias. One study of patients who had implants for various indications, including AF monitoring, cryptogenic stroke and syncope, found that rates of false-positive range from 46% to 86% depending on the indication for implantation [34]. It is therefore important the automated interpretations be checked by clinicians before making changes to patient management.

In the context of ILR for undetermined syncope, a systematic review suggests that the diagnostic yield was 43.9%, and the final proportion of subjects diagnosed with arrhythmic syncope, ventricular arrhythmias, supraventricular arrhythmias and bradyarrhythmias were 26.5%, 2.7%, 4.9% and 18.2%, respectively, but the proportion of analysable ECG recording during symptoms was only 89.5% [35].

Patient selection and pathway development are essential in understanding how ILR devices can be used in everyday practice. There are many cardiac conditions such as those highlighted in this review that can predispose patients to arrhythmias. Within each condition, clinical assessment is important, as well as any results from investigations in order to risk stratify patients. The challenge is that many professionals may review patients with palpitations and syncope, including the general practitioner, emergency department doctor, acute medical physician, geriatrician, neurologist and cardiologist, and not all of these professionals will know that ILR is an option for investigations and the local pathways that patients may be referred for consideration of these devices. The resources required to care for patients with ILR extend beyond that of physically implanting the device, also including the staff required to monitor patients and care for patients that have arrhythmias that are identified.

6. Conclusions

In conclusion, the ILR has the potential to be a valuable diagnostic tool for patients with cardiac and non-cardiac conditions as well as post-cardiac procedures. Even within different conditions, there are patients with variable severity and propensity for arrhythmias, so it is important that the risks and costs be considered against the benefit, especially when the use of cheaper alternatives, such as a cardiac Holter monitor, is possible. In cryptogenic stroke and some conditions where the risk of arrhythmia is high, the benefits of ILR to identify arrhythmia may routinely outweigh the risk, but in other scenarios, the risk of each case should be considered individually.

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