The utility of implantable loop recorders (ILR) in patient management: an age and indication stratified study in the outpatient-implant era

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Abstract

Introduction

Implantable loop recorders (ILR) are now routinely implanted for long-term cardiac monitoring in the clinic setting. This study examined the real-world performance of these devices, focusing on the management decision changes made in response to ILR-recorded data.

Methods and Results

This was a single centre, prospective observational study of consecutive patients undergoing ILR implantation. All patients who underwent implantation of a Medtronic Reveal LINQ device from September 2017 to June 2019 at Barts Heart Centre were included.

501 patients were included. 302 (60%) patients underwent ILR implantation for an indication of pre-syncope/syncope, 96 (19%) for palpitations, 72 (14%) for atrial fibrillation (AF) detection with a history of cryptogenic stroke and 31 (6%) for patients deemed to be high risk of serious cardiac arrhythmia.

The primary outcome of this study was that an ILR-derived diagnosis altered management in 110 (22%) of patients. Secondary outcomes concerned sub-group analyses by indication: in patients who presented with syncope/presyncope, a change in management resulting from ILR data was positively associated with age (HR: 1.04 [95%CI 1.02-1.06]; $p<0.001$) and negatively associated with a normal ECG at baseline (HR 0.54 [0.31-0.93]; $p=0.03$). Few patients (1/57, 2%) aged <40 years in this group underwent device implantation, compared to 19/62 patients (31%) aged 75 years and over ($p = 0.0024$). 22/183 (12%) of patients in the 40-74 age range had a device implanted.

In patients who underwent ILR insertion following cryptogenic stroke, 13/72 patients (18%) had AF detected leading to a decision to commence anticoagulation.

Conclusion

These results inform the utility of ILR in the clinical setting. Diagnoses provided by ILR that lead to changes in management are rare in patients under age 40, particularly following syncope, presyncope or palpitations. In older patients new diagnoses are frequently made and trigger important changes in treatment.

Key words:

Implantable loop recorder; cardiac monitoring; arrhythmia; syncope; palpitations; cryptogenic stroke

Introduction

Implantable loop recorders (ILRs), subcutaneous devices for long-term monitoring of heart rhythms, have become widely used for arrhythmia diagnoses. Recent iterations of guidelines have significantly expanded the accepted indications and clinical scenarios where ILRs may be deployed [1–3]. This, together with the ease of implantation of modern devices which may be safely inserted in a non-surgical clinic setting by allied healthcare professionals, has resulted in a dramatic rise in their use [4].

However despite their apparent ease of use, ILRs are a relatively expensive device with the National Health Service (NHS) tariff for implantation being £2,168. This does not capture their requirements for ongoing resources for monitoring and explantation [5]. Further under-reported burdens exist, including cosmetic effects, minor complications and psychological impacts in the young.

Although the diagnostic ability of ILRs to successfully detect arrhythmia is well established, the impact of these devices on patient pathways is under investigated. It has been established that ILRs are generally able to successfully detect an arrhythmia if it occurs[6], but data on whether ILR implantation leads to changes in patient management or outcomes is sparse.

As ILR implantation volume grows, the contexts in which ILRs may provide a substantial patient management benefit become increasingly important to define, over and above the provision of merely electrophysiological reassurance. This study aimed to define the indications and diagnostic yield of ILR implantation by examining the indications, outcomes and management of consecutive patients undergoing ILR implantation in a single, tertiary centre.

Methods

This was a single centre, prospective observational study of consecutive patients undergoing ILR implantation in our institution. The study and protocol was registered as a service evaluation project and endorsed by the Barts Health NHS Trust Clinical Effectiveness Unit, study number 10849, and confirmed to the principles of the Declaration of Helsinki.

Study population

All patients who underwent implantation of a Reveal LINQ (Medtronic Ltd, Minneapolis, MN) device via the outpatient ILR implantation service from September 2017 to June 2019 at Barts Heart Centre were included. All implants were performed by allied health professionals in the outpatient setting, as has been previously described [4]. Patients underwent routine post-implant six week telephone follow-up and thereafter six-monthly remote downloads in addition to unscheduled device downloads if symptoms or clinical events were reported, arrhythmia was detected automatically by the ILR or if a patient-triggered event occurred.

Data collection

Patient demographics, referral source and device indications were prospectively entered into a procedural database at the time of implant. Electronic patient records (Cerner Millennium, North Kansas City, MO) and remote downloads (Carelink™, Medtronic Ltd, Minneapolis, MN) were examined for follow up data.

Data analysis

Primary outcome

The primary outcome of this study was to determine the diagnostic utility of ILR device related to the original indication for insertion. This was defined as a documented diagnosis in the medical notes having been confirmed or reached through ILR monitoring resulting in a treatment or management decision or change being enacted. This was classified into no change in management, medical therapy

(defined as a change or recommendation in prescribed medication/ablation procedure), permanent pacemaker (PPM) implant or implantable cardioverter defibrillator (ICD) implant with the time-to-diagnosis also being calculated. Data was collected through examination of the electronic health record by two investigators (MMS, DMJ) and if a treatment decision was unclear, or there was uncertainty as to the ILR's contribution to achieving a diagnosis, a consensus opinion with two senior cardiologists was reached (MF, MJE).

With the primary outcome being achieved in 22% of our cohort (n=501), this study would have needed a sample size of 264 to be appropriately powered presuming 95% confidence intervals and a 5% margin of error. At a sample size of 501, the margin of error is 3.6%.

Further analysis

The reasons leading to device implant were categorised into four principal indications: pre-syncope/syncope, palpitations, atrial fibrillation (AF) detection/cryptogenic stroke, and "high risk monitoring". This latter category included patients who were considered as being indeterminate or high risk for sudden cardiac death and who were recommended for arrhythmia monitoring (e.g. severe aortic stenosis, cardiomyopathies, familial arrhythmic syndromes). Further data collected included patient's clinical history, ECG, prior cardiac monitoring, cardiac morphology and cardiac functional and imaging assessments (including reports of echocardiography, cardiac magnetic resonance, cardiac and coronary computed tomography imaging and angiography). LV functional assessments were classified into normal (left ventricular ejection fraction, LVEF ≥55%), mild impairment (LVEF <55% and ≥40%) and severe impairment (LVEF <40%)

Groups were stratified by age, indication and time-to-event (event being defined as insertion of PPM or ICD). The main secondary analysis concerned analysis of the pre-syncope/syncope indication subgroup. Survival analysis was performed to examine time-to-event stratified by age (<40, 40-74, ≥75 years of age with comparisons between groups visualised with Kaplan-Meier curves and log-rank testing being performed to compare differences between groups. A Cox proportional hazards model

was used to estimate the influence of age, sex, underlying cardiac disease and normal 12-lead ECG on likelihood of device implantation in the pre-syncope/syncope subgroup. For descriptive statistics, parametric variables were compared using Student's T-test, and data presented as mean ± SD. Non-parametric continuous variables were compared with the Mann-Whitney U test and are presented as median (range). The Chi-squared test is used to compare proportions. All analyses were conducted within the R statistical environment (R version 4.0.1). [7]

Results

There were 501 patients in the study cohort. The mean age of the study group was 56 ± 18 years, with a range of 17 to 93 years of age, 51% of who were female. The median duration of follow up was 663 days (IQR = 300-759 days). Over two-thirds of referrals (344, 69%) were from specialist cardiac electrophysiologists Detailed demographics of the entire cohort are presented in Table 1. No patients were lost to follow up and all devices were first time implants. Trend lines for the number of ILR implantations occurring by indication over time are detailed in Supplementary Figure 1.

Primary outcome: cohort diagnoses and management decisions

A new diagnosis or a diagnosis that altered management was made in 110 (22%) of patients. Time-to-diagnosis data is presented in Figure 1, with a median time to diagnosis of 119 days (range = 1-1290). 70% of diagnoses were reached within 90 days of implant, followed by a lower but relatively steady diagnostic yield.

Across the entire cohort, 41 patients (8%) underwent changes in medical therapy, 54 patients (11%) underwent cardiac device implantation (PPM or ICD), 13 (3%) underwent catheter ablation. 2 patients (0.4%) underwent PFO closure during study follow up, ILR did not change these patient's ultimate treatment but may have affected procedure timing. No changes in management were made during ILR follow-up in 391 (78%) patients. The management decisions resulting from ILR data are summarised in Figure 2.

Further data pertaining to patients ≥75 years of age, in whom pragmatic decisions are often taken regarding device therapy, are described in Supplementary Table 1.

Management decisions and diagnostic yield by indication

302 (60%) patients underwent ILR implantation for an indication of pre-syncope/syncope, 96 (19%) for palpitations, 72 (14%) for AF detection with a history of cryptogenic stroke and 31 (6%) for

patients deemed to be at high risk of serious cardiac arrhythmia. The range of phenotypes included in this latter category are detailed in Supplementary Table 2.

Syncope or pre-syncope

302 (60%) individuals underwent ILR implantation for an indication of pre-syncope or syncope. 259/302 patients referred for syncopal episodes rather than presyncope, 108 (42%) were referred with recurrent syncopal-sounding episodes. 42 patients (8.4%) had PPM/ICD insertion in this cohort (Table 2, Figure 2). 15/42 (38%) of these patients had recurrent syncope, the remainder were referrals following a single episode or due to pre-syncope.

In this subgroup, a change in management resulting from ILR data was positively associated with age (HR: 1.04 [95%CI 1.02-1.06]; p<0.001) and negatively associated with a normal ECG at baseline (HR 0.54 [0.31-0.93]; p=0.03) in those presenting with pre-syncope or syncope (Table 3).

Survival analysis examining time-to-device (PPM or ICD) for this subgroup is visualised in Figure 3. There was a significant difference in proportion of individuals receiving cardiac implantable devices related to patient age with p-value for log rank test achieving significance between all age groups ($p_{log\ rank}$ for ≥75 vs. < 40 = <0.0001, $p_{log\ rank}$ for ≥75 vs 40-74 = 0.0014, $p_{log\ rank}$ for 40-74 vs <40 = 0.019).

Only seven patients under the age of 60 and one patient under the age of 40 underwent cardiac device implantation (Figure 3). An ILR recording from a 34 year old female with a history of intermittent syncope over the preceding 5 years showed complete heart block in the context of a further syncopal event. She had an otherwise normal heart and normal resting ECG. A dual chamber pacemaker was implanted. A 40-year-old female with a pre-existing diagnosis of neurocardiogenic syncope underwent ILR insertion, a 10 second sinus pause was correlated with a syncopal episode. This patient underwent dual chamber pacemaker implantation.

5/42 patients in this subgroup who received a device were referred due to presyncope. A 45-year-old female with a confirmed diagnosis of hypertrophic cardiomyopathy and family history of sudden

cardiac death underwent primary prevention subcutaneous ICD implantation 8 months after ILR implant for an indication of presyncope. Of the further patients presenting with presyncope, four patients (all female, 64, 74, 85 and 88 years old) had significant brady arrythmias discovered on ILR recordings (Intermittent complete heart block or sinus pauses >3 seconds) and underwent pacemaker implantation.

Two further patients presenting with presyncope only underwent catheter ablation. Frequent ventricular ectopy was documented by the ILR in a 29-year-old female with a history of dilated cardiomyopathy, these ectopy had been previously documented on external Holter monitoring. A supraventricular tachycardia was documented in a 35-year-old female 30 days after implant; atrioventricular nodal tachycardia was diagnosed and treated with ablation following an electrophysiological study in this patient.

Monitoring for AF following cryptogenic stroke

72 patients (14%) underwent ILR monitoring having suffered a cerebrovascular event with no prior cause identified. All patients in this group had normal carotid dopplers, echocardiography and ECGs, save one patient with first degree heart block (PR interval 310ms) and two patients with patent foramen ovale (PFO). Of these patients, 13 (18%) were discovered to have asymptomatic paroxysmal AF, all were medically treated with anticoagulation. Of these, sinus node disease was also documented in one of these patients (82 year old female), who underwent pacemaker implantation and one further patient (2.4%, 58 years old) had nocturnal AV block and was also treated with pacemaker implantation. Two patients (4.9%) with established PFO had sinus rhythm only documented, and PFO closure was undertaken as a result. Thus ILR monitoring resulted in a change in management in 15 (21%) patients with this indication, with a median time to diagnosis of 273 [range 30 – 600] days.

Palpitations

96 patients (19%) underwent ILR implantation for prospective diagnoses of palpitations. The most common diagnoses reached in this group was pAF (16/96, 17%), with 9 patients (9%) having a diagnoses of SVT reached through ILR monitoring and 3 diagnoses (6 patients, 6%) of ventricular ectopy. 8 (8%) diagnoses of bradycardia (3 AV nodal disease, 5 sinus node disease) were confirmed in this group, resulting in five patients being treated with pacemaker implants.

Monitoring of high-risk patients

A number of implants (31 patients) were performed for those considered at high risk of cardiac arrhythmia, including patients with congenital heart disease, cardiomyopathy, previous myocarditis. Five diagnoses were made in this group: two patients with AV nodal disease, one patient with sinus node disease (all three of whom underwent PPM insertion), one patient with pAF and one patient with SVT (no medication initiated). Further details concerning patients with known cardiomyopathy and the phenotypes of patients including in the high-risk monitoring group are detailed in Supplementary Table 2.

ILR explantations

All patients included in this study were having an ILR device implanted for the first time. We reviewed explantation data from our centre for the same period of this study. The rate of a further ILR device being implanted after the initial device reaching end-of-service and being explanted was 1.8% (4/223). In our study cohort, 34 patients had had their device explanted. Of these one patient had a PPM insertion and one patient underwent AVNRT ablation, AF was detected for two patients and they received medical treatment. One patient had their device resited. The remaining 29 had no new ILR-derived diagnosis with their device having reached end of service and no replacement device was sited. The characteristics of these patients are summarised in Supplementary Table 3.

Discussion

In this study examining patient outcomes in a large, unselected population referred for ILR implantation, the key findings are:

1) implantable loop recorder data frequently leads to changes in the management of middle-aged and elderly patients presenting with unheralded syncope or pre-syncope.
2) ILR implantation only rarely changes the management or diagnosis of young patients (<40yo) presenting with syncope or presyncope.
3) A normal 12-lead ECG is significantly and negatively associated with an ILR-derived change in management in patients presenting with syncope or pre-syncope.

Our experience also confirms the substantial diagnostic utility in patients implanted with an indication of cryptogenic stroke.

The contrast between the first two key findings is highly significant. The ease of implantation and of follow-up of modern ILR devices leads to a lower threshold for recommendation of ILR monitoring and an expanding patient cohort. Indeed, in this study, all devices were implanted in an outpatient setting by nurse practitioners. The distribution of indications was also in keeping with that of previous studies [8–10].

However, it is striking that whereas in a quarter of patients over the age of 75 a treatment recommendation of pacemaker implant was made, in only two patients under the age of 40 did device implantation occur. Around a third of referrals were in this latter subgroup, and all resulting diagnoses may have been secured by recourse to alternative non-invasive monitoring rather than ILR implantation. Such non-invasive monitoring may have also been more appropriate in patients with palpitations as the indication: these individuals were not incapacitated during symptoms, and intermittent, non-invasive event monitoring would have likely been a reasonable diagnostic strategy in order to acquire symptom-arrhythmia correlation. The increasing availability of devices such as the

AliveCor Kardia (AliveCor Inc., Mountain View, CA) did not reveal any reduction in ILR implantation in our study (Supplementary Figure 1). However, data such as that from a UK emergency department providing AliveCor devices to patients attending with palpitations claim significant cost reduction per cardiac dysrhythmia diagnosis through use of these commercially-available tools[11] and suggests that head-to-head analysis of this strategy vs. ILR may be a clinically-useful exercise.

It could be expected that we find the age distribution of the diagnostic yield is heavily skewed towards the elderly population. Elderly patients are far more likely to have conduction system or atrial fibrosis, predisposing to heart block or atrial fibrillation, whereas vagal phenomena predominate in youth [12]. The small diagnostic yield in younger patients focuses attention back to the importance of clinical history taking. The few young patients in our study in whom ultimate management involved pacemaker implantation universally had stories of unheralded syncope with injury. This study has demonstrated that the yield in this younger cohort is generally low and therefore, armed with this knowledge, there is further importance attached to ensuring that precise details of the index event are gathered and reviewed to ensure that unnecessary ILR implantations are avoided.

Equally of interest is the large proportion of elderly patients (≥75 years) who avoided pacemaker implant following ILR implant despite a history of syncope or severe presyncope. Many of these patients would also fulfil guideline recommendations that pacemaker implantation would be reasonable. It is remarkable that so many elderly patients in our cohort who presented with true syncope avoided pacemaker implantation when a reasonable pragmatic clinical approach may be "to implant a pacemaker anyway"[13]. A further prospective study might aim to define whether ILR implantation has benefit in such patients over empirical pacemaker implantation in the era of outpatient ILR insertion given that numbers of pacemaker procedures continue to increase year on year[14] and meta-analysis data in patients ≥ 75 years of age has shown that they are at much increased risk of post-implant complications [15].

In patients who have had prior cryptogenic stroke, where ILR implantation was recommended for AF detection, diagnostic yield was 21%. Recently published trials such as STROKE-AF[16] and PER DIEM[17] have both demonstrated that the rate of AF detection in patients with stroke and no prior evidence of AF is much higher when compared to external modes of monitoring. The rate of AF detection in our analysis was higher than in either of these trials (12.1% and 15.3%, respectively) suggesting no significant reduction in efficacy outside of a trial environment and further suggesting strong support for ILR use in this subgroup. Further exploration of data from these patients is warranted.

Limitations

As a single centre, retrospective study results should be considered as hypothesis generating and requires confirmation in prospective, ideally randomised, studies. No guidelines with respect to qualification for ILR insertion were available at the time of ILR implantation, therefore patient selection was highly referrer dependent. The study may contain a bias towards "positive diagnosis" whereby we are looking for ILR to change management, and it was not possible to capture situations where a finding of "no arrhythmia" was beneficial to patient's care over and lifestyle advice given.

Conclusions

Our findings inform the utility of ILR implantation in the clinical setting. In this study, a majority of patients were performed for investigation of syncope or presyncope. In contrast to older patients, very few younger (<40 years of age) patients had changes in their management made as a result of data acquired from the ILR. Paroxysmal AF is detected in a high proportion of ILR patients referred following cryptogenic stroke.

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Data availability statement

The data underlying this article can be shared on reasonable request to the corresponding author.

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Table 1. Patient demographics by indication for device implantation

	Pre-syncope/ Syncope (N=302)	Palpitations (N=96)	Cryptogenic Stroke/ AF detection (N=72)	Monitoring of high-risk patients (N=31)	All Patients (N=501)
Male Gender	152 (50 %)	32 (33 %)	40 (56 %)	20 (65 %)	244 (49 %)
Age (Mean±SD)	58 ± 19	48 ± 16	61 ± 13	53 ± 19	56 ± 18
Age Group					
≥75yo	62 (21 %)	4 (4 %)	9 (12 %)	4 (13 %)	79 (16 %)
40-74yo	183 (61 %)	64 (67 %)	58 (81 %)	18 (58 %)	323 (64 %)
<40yo	57 (19 %)	28 (29 %)	5 (7 %)	9 (29 %)	99 (20 %)
Referral Source					
Cardiologist: EP specialist	216 (72 %)	63 (66 %)	43 (60 %)	22 (71 %)	344 (69 %)
Cardiologist: non-EP	78 (26 %)	33 (34 %)	12 (17 %)	9 (29 %)	132 (26 %)
Non-cardiologist	7 (2 %)	0 (0 %)	16 (22 %)	0 (0 %)	23 (5 %)
Unknown	1 (0 %)	0 (0 %)	1 (1 %)	0 (0 %)	2 (0 %)
History of Presyncope or Syncope					
Presyncope	43 (14 %)	0 (0 %)	0 (0 %)	0 (0 %)	43 (9 %)
Syncope	259 (86 %)	1 (1 %)	0 (0 %)	1 (3 %)	261 (52 %)
Comorbidities					
No pre-existing Medical Condition	152 (50 %)	29 (30 %)	45 (62 %)	8 (26 %)	234 (47 %)
Hypertension	65 (22 %)	9 (9 %)	17 (24 %)	2 (6 %)	93 (19 %)
Coronary Artery Disease	30 (10 %)	1 (1 %)	4 (6 %)	1 (3 %)	36 (7 %)
AF or Atrial Tachycardia	33 (11 %)	16 (17 %)	3 (4 %)	5 (16 %)	57 (11 %)
Structural Heart Disease	14 (5 %)	20 (21 %)	6 (8 %)	11 (35 %)	51 (10 %)
Cardiomyopathy	30 (10 %)	10 (10 %)	0 (0 %)	6 (19 %)	46 (9 %)
Other Medical Diagnosis	12 (4 %)	7 (7 %)	1 (1 %)	5 (16 %)	25 (5 %)
ECG findings at baseline					
Normal	205 (68%)	59 (61%)	48 (67%)	10 (32%)	322 (64%)
Conduction system disease	44 (15%)	15 (16%)	3 (4%)	10 (32%)	72 (14%)
Atrial fibrillation	11 (4%)	1 (1%)	1 (1%)	1 (3%)	14 (3%)
ECG unavailable	37 (12%)	16 (17%)	20 (28%)	9 (29%)	82 (16%)
Other	5 (2%)	5 (5%)	0 (0%)	1 (3%)	11 (2%)

Table 2. Management decisions for whole cohort and by indication for ILR insertion

	All Patients (N=501)	Pre-syncope/ Syncope (N=302)	Palpitations (N=96)	Cryptogenic Stroke/ AF detection (N=72)	Monitoring of high-risk patients (N=31)
Catheter ablation	13 (2.6%)	7 (2.3%)	6 (6.3%)	0 (0%)	0 (0%)
Medical treatment	41 (8.2%)	19 (6.3%)	11 (11.5%)	11 (15.3%)	1 (3.2%)
PPM/ICD insertion	54 (10.8%)	42 (13.9%)	7 (7.3%)	2* (2.8%)	3 (9.4%)
PFO closure	2 (0.4%)	0 (0%)	0 (0%)	2 (2.8%)	0 (0%)
No management change	391 (78.0%)	234 (77.5%)	72 (75.0%)	57 (79.1%)	26 (83.9%)

** Denotes that these patients also received medical therapy with anticoagulation*

Table 3. Cox proportional hazard model of likelihood of patients with presyncope or syncope having a treatment change decision dependent on results from an ILR.

	Hazard Ratio	Lower 95% CI	Upper 95% CI	z	p
Age (Years)	1.04	1.02	1.06	4.67	<0.001
Sex (Male)	0.78	0.46	1.31	-0.95	0.34
Pre-existing condition	0.70	0.41	1.19	-1.30	0.19
Normal ECG	0.54	0.31	0.93	-2.20	0.03

Age is positively associated and a normal ECG is negatively associated with ILR implantation resulting in a change in management in patients presenting with pre-syncope or syncope

Figure Legends

Figure 1

Time to diagnosis. The time to first diagnosis across the entire cohort is shown on a Kaplan-Meier plot, with 95% confidence intervals represented by dashed lines. 22% of patients received a new diagnosis or a diagnosis that altered management. 70% of diagnoses were reached within 90 days of implantation.

Figure 2

Management decisions resulting from ILR data. Changes in management following data from ILR data is illustrated. Each individual data point (patient) is represented as a circle, and is grouped into columns by age at implant. Colours represent final treatment. Data is stratified by indication.

Figure 3

Kaplan-Meier plot of cardiac implantable electronic devices (CEID) in patients with an indication of syncope or presyncope, stratified by age group. Significant differences between all three age groups ($p_{log\ rank}$ for ≥75 vs. < 40 = <0.0001, $p_{log\ rank}$ for ≥75 vs 40-74 = 0.0014, $p_{log\ rank}$ for 40-74 vs <40 = 0.019). In the age <40 years group, very few CEIDs are implanted, compared to age >75 years, where 30% of patients can expect a PPM or ICD implantation.