Implantable loop recorder is an effective diagnostic tool for unexplained syncope

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ABSTRACT

INTRODUCTION: Patients with cardiac syncope have a significantly higher mortality than patients with syncope of non-cardiac causes, while patients with syncope of unknown aetiology constitute an intermediate risk group, presumably because this group is mixed, which suggests that further diagnostic testing is warranted.

MATERIAL AND METHODS: This was a retrospective single-centre study evaluating the diagnostic yield of an implantable loop recorder (ILR) in establishing the cause of recurrent, unexplained syncope.

RESULTS: A total of 44 patients received ILR between 2007 and 2011. Follow-up data were available for 39 patients, the mean age was 63 years (range 23-94 years), 59% were female and the mean follow-up period was 349 days. The average time to first recurrence of syncope with ECG documentation was 244 days (range 11-699 days). The mean follow-up for the total population was 349 days (range 11-1,083 days) and for the group without recurrence 460 days (range 176-1,083 days). Diagnoses were obtained in 22 patients (56%) of which the cause of syncope was cardiac in 64%.

CONCLUSION: ILR was an effective tool to establish an arrhythmic cause of the recurrent, unexplained syncope, and useful in ruling out arrhythmia as a cause of syncope. New studies are needed to demonstrate whether very prolonged monitoring in case of absent recurrence may further improve the diagnostic yield. Additionally, there is much need for randomized controlled trials to investigate whether ILR-guided therapy reduces recurrence rate and mortality.

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Syncope is defined as a transient loss of consciousness characterized by rapid onset and short duration, and followed by spontaneous, complete recovery [1]. Syncope is highly prevalent and estimated to affect 42% during the lifetime [2]. Syncope is a common complaint in general practice and emergency departments and often poses a diagnostic challenge [1]. The prognosis of syncope is related to its aetiology, not its symptomatology [2]. Patients with cardiac syncope have a significantly higher mortality than patients with syncope of non-cardiac causes, while patients with syncope of unknown aetiology constitute an intermediate risk group presumably because this group is mixed, which suggests that further diagnostic testing is warranted [2].

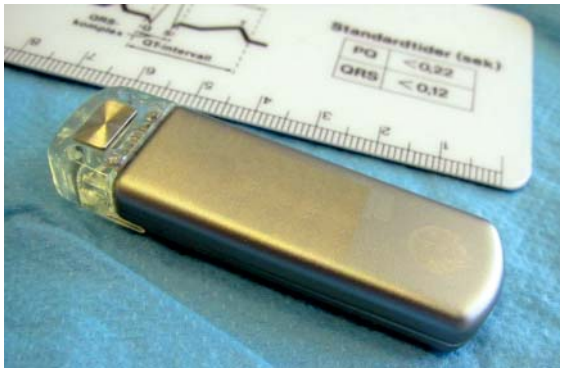
Syncope occurs infrequently and unpredictably, and patients are unlikely to be diagnosed by conventional Holter monitoring or event recording, as the chance of acquiring an electrocardiography (ECG) recording at the time of spontaneous syncope is low, even by repetitive external monitoring. The gold standard is ECG recording during a spontaneous syncope [3].

The implantable loop recorder (ILR) is a subcutaneous ECG monitoring device implanted during local anaesthetics. ILR offers up to three years of battery life. ECG is stored automatically when tachycardia, bradycardia, and asystolic pauses are detected according to pre-programmed variables. Furthermore, the patient can activate the ILR manually after a syncopal event. When the patient activates the button, the device stores the preceding six minutes of ECG by means of the loop memory.

The purpose of this study was to investigate the diagnostic value of the ILR in an unselected population in a Danish regional hospital with recurrent syncope of unknown aetiology.

MATERIAL AND METHODS

This was a retrospective, observational study of the diagnostic value of ILR performed at Herning Regional Hospital from 2007 to 2011. There were no predefined inclusion or exclusion criteria; the study thus describes the clinical practice in a single-centre during a four-year period. ILRs were used according to the current guidelines at the time of implant [1, 4]. Indications were re-



Implantable loop recorder.

ORIGINAL ARTICLE

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TABLE 1

Baseline characteristics.

	All	Diagnostic	Non-diagnostic
Women, n (%)	24 (57)	14 (64)	10 (50)
Age at first syncope, years, mean (range)	59 (20-94)	64 (21-94)	51 (20-80)
Age at ILR implant, years, mean (range)	63 (23-94)	68 (41-94)	57 (23-80)
Syncope, n (%)	37 (88)	21 (95)	16 (80)
Pre-syncope, n (%)	5 (12)	1 (5)	4 (20)
≥ 3 syncopes/pre-syncopes, n (%)	37 (88)	21 (95)	16 (80)
Ischaemic heart disease, n (%)	8 (19)	3 (14)	5 (25)
Stroke/TIA, n (%)	10 (24)	7 (32)	3 (15)
Heart failure/cardiomyopathy, n (%)	1 (2)	0 (0)	1 (5)
Heart valve disease, n (%)	2 (5)	2 (9)	0 (0)
Work-up before ILR implant, n (%)			
Cardiologist	42 (100)	22 (100)	20 (100)
Neurologist	21 (50)	11 (50)	10 (50)
Other specialist[a]	6 (14)	2 (9)	4 (20)
Holter monitoring	41 (98)	21 (95)	20 (100)
Event recording	23 (55)	11 (50)	12 (60)
Carotid sinus massage	37 (88)	20 (91)	17 (85)
Orthostatic blood pressure	17 (41)	9 (41)	8 (40)
Head-up tilt test	9 (21)	5 (23)	4 (20)
Echocardiography	40 (95)	20 (91)	20 (100)
Coronary angiography	17 (41)	10 (45)	7 (35)
CT coronary angiography	2 (5)	1 (4)	1 (5)
Myocardial perfusion scintigraphy	7 (17)	2 (9)	5 (25)
Exercise ECG	12 (29)	3 (14)	9 (45)
Electrophysiological examination	4 (10)	3 (14)	1 (5)
CT cerebrum	24 (57)	13 (59)	11 (55)
EEG	18 (43)	10 (45)	8 (40)

CT = computed tomography; ECG = electrocardiogram; EEG = electroencephalography; ILR = implantable loop recorder; TIA = transitory ischaemic attack.
a) Other specialist; otolaryngology, psychiatrist and neuropsychiatrist.

current syncope or pre-syncope of unknown aetiology. Medtronic Reveal XT/DX and two St Jude Confirm were used. Patients were followed until the first diagnostic event or for at least six months.

Time to diagnosis was described by a Kaplan-Meier curve.

The primary endpoints were incidence of diagnostic events with ECG documentation and time to diagnostic event with ECG documentation. An event was defined as recurrence of syncope or pre-syncope of similar appearance and severity as before ILR. ECG recording during recurrence was considered diagnostic when documenting arrhythmia as well as excluding arrhythmia. Both manually and automatically stored ECGs were considered. Asymptomatic arrhythmia was not considered diagnostic, except in cases of atrioventricular (AV) block or sinus arrest of a duration of more than three seconds according to the International Study on Syncope of Unknown Etiology (ISSUE) classification type 1 [3].

Trial registration: not relevant.

RESULTS

Data from the patient registry revealed 44 ILR implants in 42 different patients from 2007 to 2011. Baseline characteristics are presented in **Table 1**. **Figure 1** contains a study flowchart. The two ILR reimplants were performed due to unsatisfactory ECG quality. Two patients were excluded due to < 6 months of follow-up and one died before the first follow-up. Thus, we analysed 39 patients. One ILR was removed because of local irritation after 12 months of follow-up without events. No other complications were reported.

New events with ECG documentation were reported in 20 patients (51%). In addition, we recorded ILR-registered episodes of sinus arrest with asystole in two patients (5%) each of 6.2 and 7.5 seconds, and both were considered diagnostic.

ILR was diagnostic in 22 patients (56%) of which the cause of syncope was cardiac in 14 patients (64%). The average time to the first recurrence of syncope with ECG documentation was 244 days (range 11-699 days). Follow-up for the total population was 349 days (range 11-1,083 days), and for the group without recurrence 460 days (range 176-1,083). **Figure 2** illustrates the cumulative incidence of diagnostic events obtained by ILR.

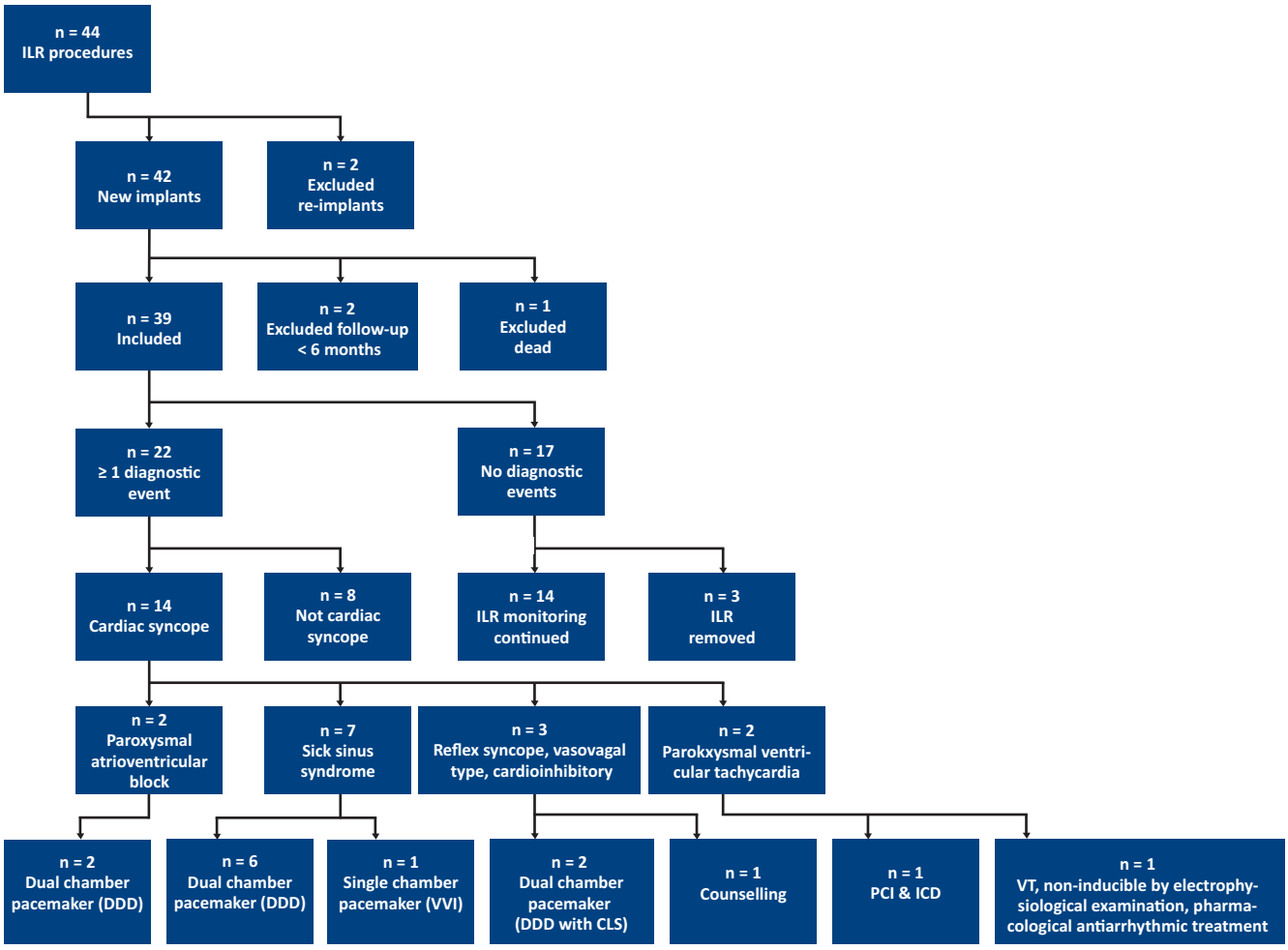
DISCUSSION

A diagnostic yield by ILR of 56% is in line with the results of previously published studies. Those studies were generally small, the patients' age and comorbidity varied and only a few were randomized [5, 6]. The rates of recurrence ranged from 38% to 59% [4-9]. The number of syncopes before ILR implant in these studies was only higher than ours in one published study [9] in which the patients on average reported 11 syncopes before ILR. This factor may have contributed to the magnitude of the diagnostic yield in this study.

In a recently published study, Furukawa et al [8] demonstrated that although the event rate was highest during the first six months of follow-up, the rate of incidence would continue a presumably linear, but lower rate from six months until the end of the study at the four-year follow-up. The cumulative rate of incidence was estimated to reach 80% at four years. The duration of the monitoring was found to be the strongest predictor for an ILR-guided diagnosis. The number of syncopes before ILR also seemed to be correlated with the probability of recurrence and with the probability of obtaining an ILR-guided diagnose, while no correlation was found with variables like age, gender, structural heart disease, syncope presentation and response to head up tilt test [3]. New studies must confirm whether the rate of incidence continues beyond the fourth year of observation. Our study could neither confirm nor question because of the small number of patients followed for more

FIGURE 1

Study flow chart.



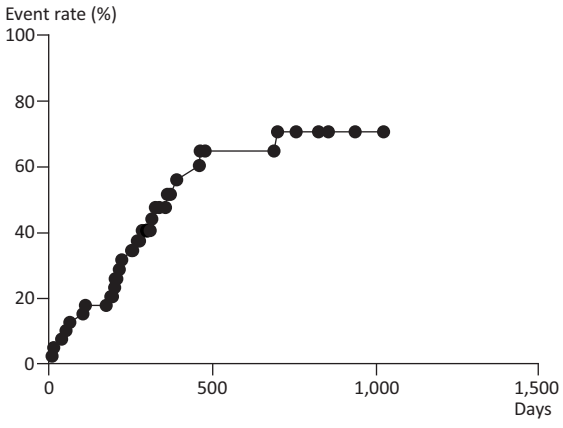
CLS = closed loop stimulation; DDD = dual chamber pacing; ICD = implantable cardioverter defibrillator; ILR = implantable loop recorder; PCI = percutaneous coronary intervention; VVI = single chamber pacing; VT = ventricular tachycardia.

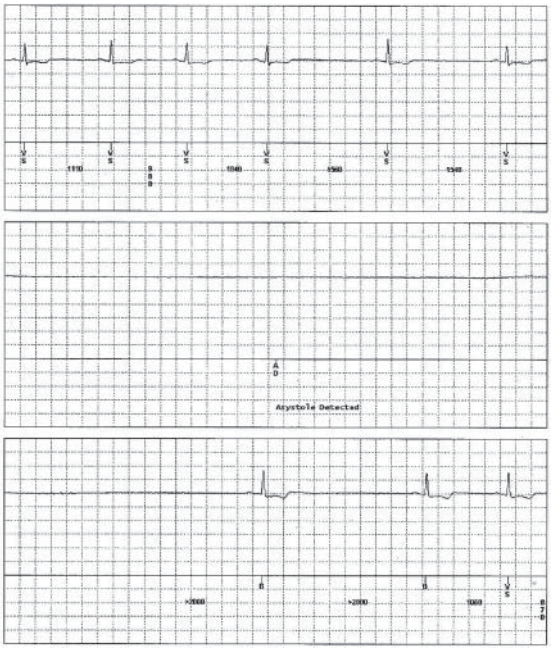
than two years. At present, we recommend to leave ILR in situ for some years in the absence of recurrence and to replace the device in case of battery depletion when the strategy of watchful waiting has been chosen.

The diagnostic outcome varies considerably depending on study design, number of patients, and duration of follow-up, and it reportedly ranges between 30% and 80% [4-9] but was, however, proven to be significant in randomized studies [5, 7]. The prevalence of asystolic pauses has proven to be high in patients with syncope of unknown aetiology despite extensive prior cardiac work-up. In addition, three patients were diagnosed with reflex syncope of vasovagal type with a significant cardioinhibitory response. Prior studies have shown that the mechanism of spontaneous syncope differs from that of provoked syncope, e.g. head-up tilt test [10], as a cardioinhibitory response more often is dem-

FIGURE 2

Kaplan-Meier curve. Cumulative event rate.





Implantable loop recorder – recording of 10.8 seconds of asystole.

onstrated by spontaneous syncope among patients primarily presenting a vasodepressor response on head-up tilt test. Development of a new ILR capable of simultaneously quantifying a drop in blood pressure would increase the diagnostic value in these cases.

An extensive cardiological and neurological workup has generally been performed before a decision is made to implant an ILR, see Table 1. ESC Guidelines recommend that IRL be considered early in patients presenting with recurring syncope of unknown aetiology and a high likelihood of recurrence within the lifetime of the battery(evidence class 1B) [1]. A strategy of watchful waiting is considered safe in those cases where guidelines are followed [1] and where patients with confirmed or suspected life-threatening arrhythmia, like patients already fulfilling the criteria for an ICD device, have been excluded [3].

Limitations

No diagnostic criteria for syncope, pre-syncope or recurrence of either of these were predefined, but assessment rested on the treating cardiologist's discretion. Patients with non-cardiac syncope and patients without recurrence of syncope may therefore have been wrongly classified, and the true value of ILR as a diagnostic tool may thus have been either over- or underestimated.

CONCLUSION

In patients with recurring unexplained syncope in a non-selected population of a medium-sized Danish Regional Hospital, ILR monitoring was found to be quite effective as a tool for diagnosis of arrhythmia as well as for ruling out arrhythmia as the cause of syncope. With a cumulative diagnostic frequency of 56% in this study, the results from the clinical implementation of ILR correspond very well to the results of previously published studies [4-9]. In accordance with current guidelines, we therefore recommend that the use of ILR be considered early in the diagnostic process in patients presenting with unexplained syncope [1]. New studies must demonstrate whether very prolonged monitoring in case of absent recurrence may improve the diagnostic yield significantly as indicated by one recently published study [8]. Furthermore, there is much need for randomized controlled trials to investigate whether ILR-guided therapy may reduce the recurrence rate and mortality.

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