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Incidence, diagnostic yield and safety of the implantable loop-recorder to detect the mechanism of syncope in patients with and without structural heart disease

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Aim To evaluate the incidence, diagnostic yield and safety of implantable loop recorders (ILRs) in patients with or without structural heart disease (SHD).

Methods and results Two-hospitals, observational, prospective study in consecutive patients with unexplained syncope who underwent an ILR implantation. Between November 1997 and December 2002, a total of 2052 patients with syncope were evaluated (referral population of 590 000 inhabitants). The diagnosis remained unexplained in 371 (18%). Of these, 103 patients (5% of total, 28% of unexplained syncope) received an ILR. SHD was present in 38 (37%), and absent in 65 (63%). During a median follow-up of 13 months, syncope was recorded in 52 patients. While patients with and without SHD had similar incidence of syncope recurrence, its mechanism was different. Patients with SHD more frequently had paroxysmal AV block and tachyarrhythmias and patients without SHD more frequently had sinus bradycardia/sinus arrest or no arrhythmia. More patients with SHD finally received an ILR-guided therapy. Sudden death occurred in one patient with SHD. Five syncope-related injuries were noted in 3 patients.

Conclusion The mechanism of syncope is different in patients with and without SHD; diagnostic yield and safety are similar in both groups. About 28% of patients with unexplained syncope have an indication to ILR implantation. The need for ILR implantation in the general population is 34 implants/million inhabitants/year.

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Introduction

The presence of structural heart disease (SHD) is the most important predictive factor for a cardiac cause of syncope, with a sensibility of 95% and a specificity of 45%, while its absence allows a cardiac cause of syncope to be ruled out in the 97% of cases.[1–2] However, this conclusion only concerns patients with a diagnosis drawn from conventional examinations. It is still unclear if the presence of SHD plays a role even in patients with syncope of unexplained aetiology. In these patients, the

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implantable loop-recorder (ILR) may be useful diagnostic device[1] although its real incidence is unknown.

Aims of this study were to evaluate the incidence, the diagnostic yield and the safety of ILR in patients with and without SHD.

Methods

This was a two-centre, prospective, observational study performed in consecutive patients who received the implantation of an ILR (Reveal or Reveal Plus, Medtronic) to detect the mechanism of otherwise unexplained syncope. According to current guidelines[1–4], we considered those patients who had severe (high risk or high frequency) syncopes that justified the need of a precise diagnosis and its specific therapy and a negative work-up eligible for ILR implantation. High risk or high frequency syncopes were considered those that: (1) were very frequent, e.g., altered the quality of life, or (2) were recurrent and unpredictable (absence of premonitory symptoms) thus exposing patients at high risk of trauma; or (3) occurred during the prosecution of a 'high risk' activity (e.g., driving, operating heavy machinery, flying, competitive athletics, etc).

After the implantation, the patients were usually discharged within 24 h, with scheduled controls every three months, unless symptoms occurred. In case of battery depletion before documentation of a syncopal relapse, patients were asked to undergo a second ILR implantation.

The primary endpoint of the study was the electrocardiographic diagnosis made by the analysis of the electrocardiographic tracing obtained during the first syncopal episode that was correctly recorded by the device. Pre-syncopal episodes were not considered. Moreover, based on clinical features and electrocardiographic tracings we derived the likely clinical diagnosis.

In particular, based on the results of ISSUE study[5–7], the mechanism of syncope was considered likely to be due to a primary cardiac arrhythmia when sudden onset AV block or bradycardia or atrial/ventricular tachyarrhythmias were detected at the time of the syncopal attack. Conversely, the mechanism of syncope was considered likely to be neurally mediated when no rhythm variations were detected in absence of other competing diagnosis or brady- or tachyarrhythmias occurred which were gradual and progressive in their onset and termination.

Statistical methods

Comparison between the two groups was performed by means of the Fisher's exact test for proportions. A P value of 0.05 or less was considered as significant. The time to the onset of events was analysed by means of the Kaplan—Meier survival curves, which were compared using the log-rank test.

Results

Between December 1997 and December 2002 a total of 2057 patients with syncopes were referred to our centres (Fig. 1). In 18% of these patients the diagnosis remained unexplained at the end of the conventional investigation. ILR was implanted in the 103 patients who fulfilled the inclusion criteria. Thus, the ILR incidence was 5% of total patients with syncope and 28% of patients with unex-
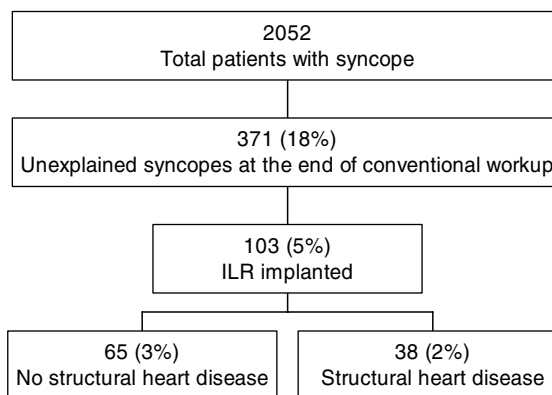

Fig. 1 Patient log.

plained syncope. There were 57 men and 46 women, with a mean age of 69 ± 11 years and had an individual rate of 11 ± 5 syncopes. Among ILR patients, SHD was present in 38 patients (37%): previous myocardial infarction in 12 patients (11%), dilated cardiomyopathy in 6 patients (6%), valvular heart disease in 1 patient (1%), and bundle branch block in 26 patients (25%).

Overall, during a median follow-up of 13 months (interquartile range 6-23), an ECG-documented syncope occurred in 52 patients with an actuarial rate of 21% (95% CI 17—25%) at 1 year and 53% (95% CI 47—59%) at 2 years. The Kaplan—Meier's recurrence curves were similar in the patients with and without structural heart disease (log-rank test, $P = 0.78$), (Fig. 2). Another 4 patients experienced a syncope, but they were unable to activate the ILR. In 3 cases, a second ILR was needed, due to battery exhaustion of the first device.

Among the 38 patients with SHD, 22 (58%) had an electrocardiographic recording during syncope (Table 1). All but two had an arrhythmia at the time of the syncope. The most frequent arrhythmia was a paroxysmal (10 patients) or persistent (3 patients) AV block, reported in 34% of cases. The three cases of persistent AV block were documented by standard ECG. Atrial tachycardia occurred in 8%, sinus bradycardia/sinus arrest in 5%, ventricular tachycardia/fibrillation in 5% of cases. The 2 patients with ventricular tachycardia/fibrillation were promptly rescued and survived the event.
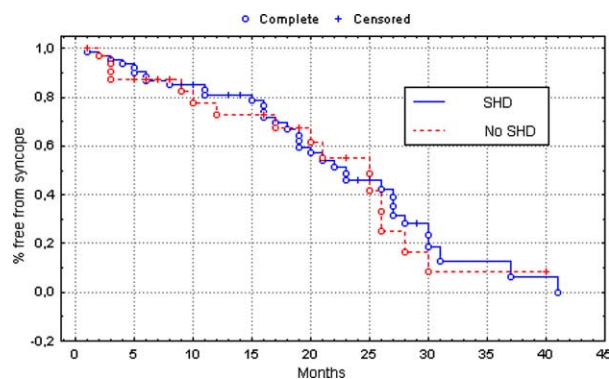

Fig. 2 Actuarial curves of ECG-documented recurrence of syncope in patients with or without SHD.

Table 1 Electrocardiographic diagnosis

	SHD (n = 38)	No SHD (n = 65)	P value
Total patients with ECG recordings	22 (58%)	30 (45%)	0.17
Persistent/paroxysmal AV block	13 (34%)	8 (13%)	0.01
Sinus bradycardia, sinus arrest	2 (5%)	11 (15%)	0.07
Atrial tachycardia	3 (8%)	0 (0%)	0.05
Ventricular tachycardia/fibrillation	2 (5%)	0 (0%)	0.13
No arrhythmia	2 (5%)	11 (17%)	0.07

SHD, structural heart disease.

Table 2 Final clinical diagnosis

	SHD (n = 38)	No SHD (n = 65)	P value
Total diagnosis	22 (58%)	33 (51%)*	0.50
Primary cardiac arrhythmia likely	18 (47%)	10 (15%)	0.0001
Neurally mediated syncope likely	4 (10%)	20 (31%)	0.02
Hysteria	0 (0%)	2 (2%)	0.40
Epilepsy	0 (0%)	1 (1%)	0.63

SHD, structural heart disease.
*In three patients, the diagnosis was made by means of standard ECG.

The final clinical diagnosis (Table 2) was primary cardiac arrhythmia in 20 cases (52%), neurally mediated syncope in 2 cases (5%). In 43% of cases, the diagnosis remained unexplained despite ILR.

Among the 65 patients without SHD, 30 (45%) had an electrocardiographic recording during syncope (Table 1). Three findings were frequently found: normal cardiac rhythm in 17% of cases, sinus bradycardia/sinus arrest in 15% of cases and paroxysmal or persistent AV block in 13% of cases.

In 3 other patients the diagnosis was made during the follow-up on a clinical basis in absence of ILR recording; this was hysteria in 2 cases and epilepsy in 1 case. Thus, in total a clinical diagnosis was made in 33 patients (51%) (Table 2) comprising primary cardiac arrhythmia in 10 cases (15%), neurally mediated syncope in 20 cases (31%), hysteria in 2 cases (2%) and epilepsy in 1 case (1%).

In comparison with patients with SHD, AV block and tachycardia were significantly less common in patients without SHD, whereas a normal rhythm and sinus bradycardia/sinus arrest were more frequent (Table 1). Also the final clinical diagnosis differed significantly between patients with and without SHD (Table 2).

Therapy

An ILR-based therapy was prescribed in 39 patients (38%) (Table 3), with pacemaker implantation performed in the majority; 62% of all enrolled patients did not receive any therapy and significantly fewer patients without SHD required a treatment.

Adverse events

During the follow-up 4 patients died, one of them with SHD died of sudden death, whose recording is unavailable; the others died of an extracardiac cause (lung insufficiency, Grawits cancer, pulmonary embolism). Syncope-related traumatic episodes were 5 and occurred in 3 patients.

Discussion

Our results show that ILR permitted the diagnosis in approximately half of the patients with a similar percentage in patients with and without SHD. These data are higher

Table 3 ILR-based therapy

	SHD (n = 38)	No SHD (n = 65)	P value
Any therapy	20 (54%)	19 (28%)	0.02
Pacemaker	14 (37%)	14 (21%)	0.07
Implantable defibrillator	1 (3%)	0 (0%)	0.37
Catheter ablation	1 (3%)	0 (0%)	0.37
Others (drugs, by-pass graft)	4 (11%)	5 (7%)	0.43
No therapy	18 (46%)	46 (72%)	0.02

SHD, structural heart disease.

than some previous studies in which a ILR diagnosis ranged from 17% to 42%[5–7], but lower than in others in which an ILR based diagnosis was made in 58%[8] and 94%.[9]

Diagnostic value and safety of ILR-guided therapy

The electrocardiographic mechanism and the aetiology of syncope differ significantly in patients with and without SHD. While the ILR showed a similar diagnostic yield in both groups, more than half of the patients with SHD had a primary cardiac arrhythmia whereas 15% of patients without SHD had a syncope due to this mechanism. Nevertheless, a percentage of 15% of primary cardiac arrhythmic cause in patients without SHD is not negligible and is higher that observed by means of the conventional investigation which was 3%.[2] The high incidence of a primary cardiac arrhythmia in patients with SHD confirms the results of previous studies which evaluated patients with SHD and a negative electrophysiological study.[5,6] As expected, neurally mediated syncope, occurred three times less frequently in patients with SHD than in patients without SHD. Thus, our results corroborate the value of underlying SHD to predict a cardiac cause of syncope also in patients with unexplained syncope at the end of conventional evaluation.

We had a case of sudden death and traumatic syncopal relapses were extremely low. Therefore, ILR use also seems reasonably safe in patients with SHD, as shown in a previous study.[7]

Impact of ILR-strategy on the management of syncope

We observed that 5% (2% with and 3% without SHD) of all patients referred for evaluation of syncope finally received an ILR-based evaluation (Fig. 1). The corresponding figure of patients with unexplained syncope at the end of conventional work-up is 28% (10% with and 18% without SHD).

ILR-guided therapy was performed in a total of 39 (38%) patients, corresponding to 10.5% of all patients with unexplained syncope at the end of the conventional work-up (Table 3 and Fig. 1). A therapy was more likely adopted in patients with SHD than in those without.

Since the overall population of the districts of the two enrolling hospitals is 590 000 inhabitants and the implant rate was 20 ILR per year, we estimate that the need for ILR implantation in the "real world" is 34 implants/million inhabitants/year, using our current indications. One-third of implantations are reserved to patients with SHD. To our knowledge, this is the first study which has attempted to calculate the ILR requirement in the unselected general population.

Conclusions

This study shows that the mechanism of unexplained syncope is different in patients with and without SHD, though diagnostic yield and safety are similar in both groups. A cardiac cause may also be present in a non-negligible percentage of patients without SHD.

Based on our current indications, about 28% of patients with unexplained syncope finally received an ILR implantation and we estimated that the need for ILR implantation in the general population is 34 implants/million inhabitants/year.

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