Utility of Implantable Loop Recorders for Diagnosing Unexplained Syncope in Clinical Practice

Address for correspondence:
Felipe R. Entem, MD
Cardiology Departament
HU Marqués de Valdecilla
Av. Valdecilla sn
39003 Santander, Cantabria, Spain
fentem@eurodivisas.com

Felipe R. Entem, MD, Susana G. Enriquez, MD, Manuel Cobo, MD, Víctor Expósito, MD, Miguel Llano, MD, Marta Ruiz, MD, Juan Jose Olalla, MD, Macarena Otero-Fernandez, MD

Cardiology Department, HU Marqués de Valdecilla, Santander, Cantabria, Spain

ABSTRACT

Background: Establishing a symptom–rhythm correlation in patients with unexplained syncope is complicated because of its sporadic, infrequent, and unpredictable nature. Prolonged monitoring with an implantable loop recorder (ILR) allows the recording of electrocardiogram (ECG) data from a spontaneous syncopal event.

Hypothesis: The aim of this study was to evaluate the usefulness of the ILR for the diagnosis of syncope of unknown origin after conventional management in clinical practice.

Methods: We reviewed the results with ILR implantation in patients with syncope of unknown origin after conventional management in the cardiology department at HU Marques de Valdecilla (Santander, Cantabria, Spain).

Results: One hundred and forty patients (age 64 ± 16 y; 86 male [62%]) with syncope of unknown etiology after conventional work-up underwent prolonged monitoring with an ILR from September 1998 to February 2006; 46 patients (33%) had structural heart disease. During a mean follow-up of 346 ± 160 d, 51 patients (36.5%) had recurrent syncope with diagnostic ECG recording. An arrhythmic cause for syncope was found in 33 of them (64.5%), with bradycardia present in 27 (53%) and tachycardia in 6 (11%). There were no sudden deaths, and 1 patient suffered a complication related to a recurrence of syncope.

Conclusion: Long-time experience with the ILR confirmed the utility of this device in the diagnosis of unexplained syncope in clinical practice. Most of these patients had syncope of arrhythmogenic etiology that could be successfully treated. This strategy of prolonged monitoring is safe even in patients with structural heart disease.

Key words: syncope, arrhythmia, diagnosis

Introduction

Recurrent unexplained syncope and presyncope comprise approximately 1%–6% of emergency room visits, and approximately 1% of hospital admissions.^{1,2} The estimated incidence of self-reported syncope is 6.2 of 1,000 persons/y in the Framingham study.³ The overall incidence is approximately 3%–6% over 10 y, and in a select group of patients, the prevalence of syncope could reach almost 50%.⁴

The current approach to the investigation of patients with unexplained syncope involves short-term electrocardiogram (ECG) monitoring, or provocative examination with head-up tilt and electrophysiological testing.^{5–8} A symptom–rhythm correlation is often difficult to obtain during spontaneous episodes because of the sporadic, infrequent, and unpredictable nature of syncope. Despite a wide array of diagnostic tools, including tilt-table and electrophysiological testing, the cause of syncope is not determined in a large proportion of patients.^{9–11}

Recent advances in implantable loop recorder (ILR) technology have permitted implantation of a subcutaneous nonvascular device to provide long-duration electrocardiographic monitoring, improving the overall diagnostic yield in patients with recurrent infrequent episodes of syncope.^{12,13}

The aim of the present study was to review our experience with ILR in identifying the etiology of recurrent unexplained syncope in a large series of patients after conventional management.

Methods

Patients

We included all patients with syncope referred to the cardiology department at HU Marqués de Valdecilla (Santander, Cantabria, Spain) between September 1998 and February 2006. All patients referred with this diagnosis routinely underwent a syncope protocol that included a history, physical examination, 12-lead ECG, routine laboratory investigation, and 24-h ambulatory ECG recording. Echocardiography, tilt-table tests, and an electrophysiological study were performed at the discretion of the attending physician. Patients with undiagnosed syncope after this assessment underwent implantation of an ILR if they had had 2 or more witnessed episodes of syncope of unknown origin in the previous 12 mo, or 1 episode of syncope with significant trauma or structural heart disease. Oral and written informed consent was obtained from every patient.

Loop Recorder Implantation

Two types of ILRs, Reveal and Reveal Plus (Medtronic, Inc., Minneapolis, Minn., USA), were used. The ILR was positioned subcutaneously in the left pectoral region under local anesthesia. The device recorded a bipolar ECG signal and stored it in a circular memory buffer that was frozen by the patient after a syncope episode using a handheld activator. The episodes could be downloaded after interrogation with a standard Medtronic pacemaker programmer. Some devices (Reveal Plus) have programmable automatic detection of high- and low-heart-rate episodes, which is helpful when patients are unable to activate the device or are noncompliant. Gain and sensitivity were programmed according to the manufacturer's recommendations. The device was set to record 1 patient activation and 10 automatic activations. Automatic activation was programmed for a ventricular pause of >3 sec, a ventricular rate of <40 beats/min, or a ventricular rate >180 beats/min for more than 16 beats. Of the 140 patients, 34 received Reveal ILR, and the remainder had a Reveal Plus device implanted.

Follow-up

Each patient was regularly followed by the Arrhythmia Unit. If patients had recurrence of symptoms, they were seen prior to their scheduled follow-up visit. During follow-up, loop recorders were interrogated and the data evaluated. The device remained implanted until a diagnostic event was recorded or until the end of the battery life.

Results

One hundred and forty patients with unexplained syncope had an ILR inserted. Patient characteristics and diagnostic tools are summarized in Table 1.

Recurrences

Symptoms recurred in 54 patients (38.5%) 127 d after ILR insertion (median 105 d). Failure to appropriately activate after symptoms occurred in 15 patients (28%). Five of these patients had an appropriate freeze after spontaneous symptoms on a different occasion, and in 7 patients there was automatic activation at the moment of the syncopal event. A final diagnosis was obtained in 51 patients (36.5%).

Heart Rhythm During Event

An arrhythmia was seen in 33 of the 51 patients who recorded an event (64.5%). Bradycardia was the most frequent etiology (Table 2). All bradycardic patients had their ILRs removed and permanent pacemakers inserted if necessary.

Six patients had tachyarrhythmias associated with recurrent symptoms: sustained supraventricular tachycardia in 2 patients (1 nodal-reentry supraventricular tachycardia [SVT] and 1 fast atrial fibrillation) and ventricular tachycardia in 4 patients. All tachyarrhythmias were treated

TABLE 1: Patient characteristics

Number of patients	140
Age (y), mean±SD	64±16
Sex, male	86 (62%)
Syncope in the previous 12 mo, mean±SD	2.6±1.5
Associated with structural heart disease	46
Ischemic	19
Dilated	13
Hypertrophic	4
Valvular	7
Others	3
Investigations before implantation	
Holter monitor	140 (100%)
Echocardiography	124 (88%)
Head-up tilt test	76 (46%)
Electrophysiological study	87 (62%)
Abbreviation: SD = standard deviation.	

TABLE 2: Findings at time of syncope

Normal sinus rhythm	18
Slow rhythms	27
Asystolic pause	16
Heart block	9
Sinus bradycardia (<40 bpm)	2
Fast rhythms	
Supraventricular tachycardia	2
Ventricular tachycardia	4

successfully by ICD implantation, radiofrequency ablation, and/or medication.

The remaining 18 patients had sinus rhythm during the activation episode and follow-up was continued. Devices remained implanted in these patients to monitor subsequent episodes, but none of them had a different rhythm during a mean follow-up of 466±41 d.

Follow-up

One patient developed an infection of the device during the first month after implantation. Removal of the device was performed, and the patient did well afterward. There were no other device-related adverse events.

There were 7 deaths (0.05% mortality) during the study, with a mean follow-up of 346 ± 160 d. No patient died suddenly. One patient suffered cranial trauma secondary to a syncope spell. In this case, structural heart disease was previously ruled out, and an electrophysiologic study was performed due to a left bundle branch block in a basal ECG, with no pathological findings.

Patients with Structural Heart Disease

Forty-six patients (33%) had structural heart disease (Table 1). The mean ejection fraction was $47\% \pm 13\%$. An electrophysiological study was done in 38 patients (81%). In this group, a final diagnosis was obtained in 14 patients (30%): 7 patients had sinus node dysfunction, 3 patients had complete heart block, 2 patients had ventricular tachycardia, and 2 patients were in sinus rhythm. None of these patients died suddenly during the follow-up.

Discussion

The main finding of this study was that recurrence of symptoms occurs in one third of patients in whom an ILR was implanted due to recurrent syncope of unknown etiology after a conventional work-up. Monitoring with this device is effective in establishing a symptom–rhythm correlation. In patients with recurrent syncope, around one third of them showed a normal heart rhythm during syncope, whereas the other two thirds demonstrated bradycardia or tachycardia. This retrospective single-center study represents one of the larger experiences using the ILR to investigate unexplained syncope, and represents the use of this device in routine clinical practice.

The etiology of recurrent syncope is difficult to determine if the electrophysiological and neurological work-up is negative.^{1,9} Despite the good prognosis of patients whose investigations are negative, syncope may recur with attendant morbidity and even mortality.^{14–17} Previous experience demonstrates that the ILR is an excellent diagnostic tool in the diagnosis of unexplained syncope. In the mid-1990s, the first nonrandomized study by Krhan et al.¹⁸ demonstrated the clinical value of the ILR in the investigation of syncopal patients who, despite extensive investigation, had remained undiagnosed. In several studies, Holter monitoring and external loop recording were 10% successful in obtaining ECG tracings during a syncopal event,^{19,20} whereas the ILR was 80% successful.^{21,22} The ILR has also been shown to be more likely to provide a diagnosis than conventional testing in patients with unexplained syncope.²³ In our series, the ILR was successful in establishing a symptom–rhythm correlation in 36.5% of patients. This is lower than that in other published series.^{12,13,21,22,24,25} This finding is probably a result of the inclusion of a non-previously selected population, coming from conventional management in a cardiology department, and could reflect the diagnostic value of ILR in real life.

The rhythm profile of patients during recurrent syncope reflected an arrhythmic cause in 33 patients. Twenty-six of these patients had bradycardia and 7 patients had tachycardia (2 supraventricular tachycardia and 5 ventricular tachycardia). In the remaining patients, an arrhythmia was eliminated as a potential cause of symptoms, alleviating concerns about a life-threatening arrhythmia. This is similar to the ratio of bradycardias and tachycardias in other studies,^{12,13,21,22,24,25} with predominance of slow rhythms even in patients with structural heart disease in whom a ventricular tachycardia was unlikely.²⁶

Failure to appropriately activate the device after syncope does not represent an important problem with the use of self-activating systems. Fifteen patients failed to activate the system after recurrent symptoms, but 7 of them had automatic activation at the moment of syncope, and 5 patients activated the system on a different occasion. Only 3 patients remain undiagnosed after complete follow-up.

There were no deaths and minimal complications from the implantation of the device. During follow-up, mortality was very low and no patient died suddenly. These results suggest that ILR implantation after syncope is a safe approach. The major determinant of prognosis in syncopal patients is the presence of structural heart disease.⁷ Forty-six patients had some structural heart disease in our series. Even in these subjects, if prior investigation including electrophysiological testing when appropriate screened out patients at high risk, the ILR is a low-risk option for the investigation of unexplained syncope.

Conclusions

Our study confirmed the utility of an ILR in the diagnosis of patients with unexplained syncope after conventional work-up in clinical practice. A symptom–rhythm correlation could be established in more than one-third of patients. Most of these patients had arrhythmogenic etiology to their syncope, with a predominance of slow rhythms. This strategy of prolonged monitoring is safe even in patients with structural heart disease.

References

- Day SC, Cook EF, Funkenstein H, Goldman L: Evaluation and outcome of emergency room patients with transient loss of consciousness. *Am J Med* 1992;73:15–23
- Kapoor WN: Evaluation and outcome of patients with syncope. *Medicine* 1990;69:160–175
- Soteriades ES, Evans JC, Larson MG, Chen MH, Chen L, et al.: Incidence and prognosis of syncope. *N Engl J Med* 2002;347:878–885
- Shen WK, Decker WW, Smars PA, Goyal DG, Walker AE, et al.: Syncope evaluation in the emergency department study (SEEDS): a multidisciplinary approach to syncope management. *Circulation* 2004;110:3636–3645
- Kapoor WN, Hammill SC, Gersh BJ: Diagnosis and natural history of syncope and the role of invasive electrophysiologic testing. *Am J Cardiol* 1989;63:730–734

6. Sra JS, Anderson AJ, Sheikh SH, Avitall B, Tchou PJ, et al.: Unexplained syncope evaluated by electrophysiologic studies and head-up tilt testing. *Ann Intern Med* 1991;114:1013–1019
7. Kapoor WN, Karpf M, Wieand S, Peterson JR, Levey GS, et al.: A prospective evaluation and follow-up of patients with syncope. *N Engl J Med* 1983;309:197–204
8. Manolis AS, Linzer M, Salem D, Estes NA 3rd: Syncope: current diagnostic evaluation and management. *Ann Intern Med* 1990;112:850–863
9. Martin GJ, Adams SL, Martin HG, Matthews J, Zull D, et al.: Prospective evaluation of syncope. *Ann Emerg Med*. 1984;13:499–504
10. Krahn AD, Klein GJ, Norris C, Yee R: The etiology of syncope in patients with negative tilt table and electrophysiological testing. *Circulation* 1995;92:1819–1824
11. Garcia-Civera R, Ruiz-Granell R, Morell-Cabedo, San Juan-Mañez R, Perez-Alcala F, et al.: Selective use of diagnostic tests in patients with syncope of unknown cause. *J Am Coll Cardiol* 2003;41:787–790
12. Krahn AD, Klein GJ, Yee R, Takle-Newhouse T, Norris C: Use of an extended monitoring strategy in patients with problematic syncope. *Circulation* 1999;99:406–410
13. Farwell DJ, Freemantle N, Sulke AN: Use of implantable loop recorders in the diagnosis and management of syncope. *Eur Heart J* 2004;25:1257–1263
14. Sra JS, Anderson AJ, Sheikh SH, Avitall B, Tchou PT, et al.: Unexplained syncope evaluated by electrophysiologic studies and head-up tilt testing. *Ann Intern Med* 1991;114:1013–1019
15. Klein GJ, Gersh BJ, Yee R: Electrophysiologic testing: the final court of appeal for diagnosis of syncope? *Circulation* 1995;92:1332–1335
16. Morady F, Shen E, Schwartz A, Hess D, Bhandari A, et al.: Long term follow-up of patients with recurrent unexplained syncope evaluated by electrophysiologic testing. *J Am Coll Cardiol* 1983;2:1053–1059
17. Muller T, Roy D, Talajic M, Lemery R, Nattel S, et al.: Electrophysiologic evaluation and outcome of patients with syncope of unknown origin. *Eur Heart J* 1991;12:139–143
18. Krahn AD, Klein GJ, Norris C, Yee R: The etiology of syncope in patients with negative tilt table and electrophysiological testing. *Circulation* 1995;92:1819–1824
19. DiMarco JP, Philbrick JT: Use of ambulatory electrocardiographic (Holter) monitoring. *Ann J Med* 1990;113:53–11368
20. Fogel RI, Evans JJ, Prystowsky EN. Utility and cost of event recorders in the diagnosis of palpitations, presyncope and syncope. *Am J Cardiol* 1997;79:207–208
21. Nierrop PR, Van Mechelen R, Van Elsacker A, Luijten RH, Elhendy A: Heart rhythm during syncope and presyncope: results of implantable loop recorders. *PACE* 2000;23:1532–1538
22. Ashby DT, Cehic DA, Disney PJ, Mahar LJ, Young GD: A retrospective case study to assess the value of the implantable loop recorder for the investigation of undiagnosed syncope. *Pacing Clin Electrophysiol* 2002;25:1200–1205
23. Krahn AD, Klein GJ, Yee R, Skanes AC: Randomized assessment of syncope trial: conventional diagnostic testing versus a prolonged monitoring strategy. *Circulation* 2001;104:46–51
24. Moya A, Brignole M, Menozzi C, Garcia-Civera R, Tognarini S, et al.; International Study on Syncope of Uncertain Etiology (ISSUE) Investigators: Mechanism of syncope in patients with isolated syncope and in patients with tilt-positive syncope. *Circulation* 2001;104:1261–1267
25. Inamdar V, Mehta S, Juang G, Cohen T: The utility of implantable loop recorders for diagnosing unexplained syncope in 100 consecutive patients: five-year, single-center experience. *J Invasive Cardiol* 2006;18:313–315
26. Menozzi C, Brignole M, Garcia-Civera R, Moya A, Botto G, et al.: International Study on Syncope of Uncertain Etiology (ISSUE) Investigators: Mechanism of syncope in patients with heart disease and negative electrophysiologic test. *Circulation* 2002;105:2741–2745