

Syncope

(Ital Heart J 2004; 5 (Suppl 1): 152S-155S)

© 2004 CEPI Srl

ROLE OF IMPLANTABLE LOOP RECORDER IN THE MANAGEMENT OF SYNCOPE PATIENTS

Maurizio Santomauro, Luca Ottaviano,
Alessio Borrelli, Massimo Chiariello

*Department of Cardiology, "Federico II" University,
Naples, Italy*

Syncope is a common occurrence accounting for approximately 6% of hospital admissions yet it remains one of the most difficult problems for a physician to attribute a cause. It is defined as a transient loss of consciousness and postural tone caused by a reduction in cerebral blood flow. The major obstacles to diagnosis are the unpredictable and infrequent nature of events and the high spontaneous remission rate. Syncope continues to be a diagnostic challenge in the remaining patients with a negative tilt table test. Advances in long-term cardiac monitoring techniques with the implantable loop recorders (ILR) have added a powerful tool in the field for arrhythmia detection. The ILR is suitable in patients with infrequent recurrent syncope because it permits prolonged monitoring without external electrodes. The recorded bipolar ECG signal is stored in a circular buffer. The memory buffer is frozen using a hand-held activator provided to the patient. The literature clearly supports the use of the ILR in patients with recurrent unexplained syncope who have failed a non-invasive work-up and continue to have syncope. The optimal patient for prolonged monitoring has frequent recurrent symptoms suspicious for arrhythmia. After clinical assessment including determination of left ventricular function, a decision must be made if the clinical presentation is potentially life-threatening. Loop recorders have significantly improved the ability to obtain rhythm symptom correlation physiologic data during spontaneous symptoms in patients with unexplained syncope. The ILR is a particularly useful tool for investigating patients with recurrent unexplained syncope when non-invasive tests are negative. The clinician should consider early use of the ILR when an arrhythmia is suspected, focusing on patients with a heavy syncope burden who are likely to experience recurrence.

Syncope is a common occurrence accounting for approximately 6% of hospital admissions yet it remains one of the most difficult problems for a physician to attribute a cause. It is defined as a transient loss of consciousness and postural tone caused by a reduction in cerebral blood flow¹. The major obstacles to diagnosis are the unpredictable and infrequent nature of events and the high spontaneous remission rate. Tilt table testing is the most often used diagnostic approach to patients with recurrent syncope of unknown origin and no structural heart disease, to verify a vasovagal etiology of their syncopal attacks². The frequency of a positive test result depends on the patient selection and the protocol used for tilt table testing. Several recent studies reported positive test results in 6 to 8% of controls. Patients had positive test results without pharmacological provocation in 34 to 39%, after isoproterenol provocation in 47 to 52%, and after nitroglycerin provocation in 71 to 73%³. However, syncope continues to be a diagnostic challenge in the remaining patients with a negative tilt table test. Advances in long-term cardiac monitoring techniques with the implantable loop recorders (ILR) added a powerful tool in the field for arrhythmia detection. The ILR is suitable for patients with infrequent recurrent syncope because it permits prolonged monitoring without external electrodes. The only commercially available ILR (Fig. 1) at this time is manufactured by Medtronic (Reveal, Minneapolis, MN, USA). The ILR has a pair of sensing electrodes 3.7 cm apart on the shell, measures $6.1 \times 1.9 \times 0.8$ cm, weighs 17 g, and has a battery life of 14 months. It is inserted subcutaneously in the left chest using standard sterile technique and local anesthetic. It has been implanted in the right or left parasternal, subcostal and axillary regions with an adequate, albeit lower, amplitude signal. The recorded bipolar ECG signal is stored in a circular buffer capable of retraining 21 min of uncompressed or 42 min of compressed signal in



Figure 1. The implantable loop recorder Reveal Plus.

one or three divided parts. Because the compressed signal quality is negligibly different from the uncompressed signal, it is used most often to maximize the memory capacity of the device. The memory buffer is frozen using a hand-held activator provided to the patient. The episodes (Fig. 2) are downloaded after interrogation with a standard Medtronic 9790 pacemaker programmer. The current version of the device (Reveal Plus) has programmable automatic detection of high and low rate episodes and pauses. The resultant memory configuration allows for division of multiple 1 min automatic rhythm strips in addition to one-three manual recording. This permits automated back-up of manual activation to detect pre-specified extreme heart rates or pauses (typically < 30 and > 160 b/min, and pauses > 3 s) (Fig. 3). This also permits detection of asymptomatic heart rate changes that may influence clinical judgment as to the likely cause for syncope in the absence of symptomatic recurrence.

The REVEAL investigators⁴ studied 85 patients with 5.1 ± 5.5 syncopal events within the last year. A tilt table test was performed in only 49% of the patients. During a follow-up of 11 ± 4 months, recurrent syncope or presyncope was reported in 50 (59%) patients. In three recent studies from the ISSUE investigators, ILR were implanted in three different groups of syncope patients to assess the spontaneous rhythm during spontaneous syncope after conventional testing⁵⁻⁷. The first study performed tilt tests in 111 patients with unexplained syncope suspected to be vasovagal, and ILR after the tilt test regardless of results. Syncope recurred in 34% of patients in both the tilt-positive and tilt-negative group, with marked bradycardia or asystole the most common recorded arrhythmia during follow-up (46 and 62% respectively). The heart rate response during tilt testing did not predict spontaneous heart rate during episodes, with a much higher incidence of asystole noted than expected based on tilt response where a marked cardioinhibitory response was uncommon. This study suggests that tilt testing is poorly predictive of rhythm find-

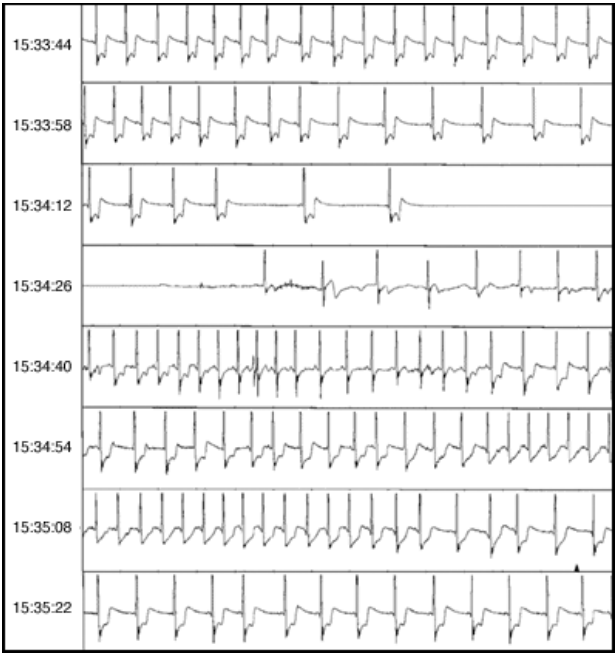


Figure 2. Download rhythm strip from an insertable loop recorder implanted in a man with recurrent unexplained syncope. Marked bradycardia followed by a 10 s pause.

ings during spontaneous syncope, and that bradycardia is more common in this population than previously recognized.

The second part of the ISSUE study performed long-term monitoring in 52 patients with syncope and bundle branch block with negative electrophysiologic testing⁷. Syncope recurred in 22 of the 52 patients with conduction system disease. Long-term monitoring demonstrated marked bradycardia mainly attributed to complete atrioventricular block in 17 patients, while it excluded atrioventricular block in 2. Three patients did not properly activate the device after symptoms. This study confirmed the previous view that negative electrophysiologic testing does not exclude intermittent complete atrioventricular block, and that prolonged monitoring or consideration of permanent pacing is reasonable in this population.

The third part of the ISSUE study examined the spontaneous rhythm in 35 patients with syncope and overt heart disease who had negative electrophysiologic testing⁵. The underlying heart disease was predominantly ischemic heart disease or hypertrophic car-

Bradycardia Rates	Tachycardia Rates	Asystole Periods
<30 bpm <40 bpm* } 4 consecutive intervals	Off >115 bpm >125 bpm >145 bpm >165 bpm* >180 bpm >210 bpm >230 bpm } Choice of 16* or 32 consecutive intervals	> 3.0 sec* > 4.5 sec

* Default Settings

Figure 3. Reveal plus automatic detection options. Reveal plus has programmable automatic detection of high and low rate episodes and pauses. The resultant memory configuration allows for division of multiple one-minute automatic rhythm strip in addition to 1-3 manual recording. This permits automated backup of manual activation to detect prespecified extreme heart rates or pauses (typically < 30 b/min, > 160 b/min and pauses > 3 s).

diomyopathy with moderate left ventricular dysfunction. Although previous studies have suggested that patients with negative electrophysiologic testing have a better prognosis there remains concern regarding the risk of ventricular tachycardia in this group. Importantly, only 2 of the 35 patients had severe left ventricular dysfunction (ejection fraction < 30%) that would have made them candidates for primary prevention of sudden death in keeping with the MADIT II trial⁸. Symptoms recurred in 19 of the 35 patients (54%), with bradycardia in 4, supraventricular tachyarrhythmias in 5, and ventricular tachycardia in only 1 patient. There were no sudden deaths during 16 ± 11 months of follow-up. This supports a monitoring strategy in patients with left ventricular dysfunction related to ischemic heart disease when electrophysiologic testing is negative.

Krahn et al.⁹ prospective randomized trial compared early use of the ILR for prolonged monitoring to conventional testing in patients undergoing a cardiac work-up for unexplained syncope. Sixty patients (33 males, 27 females, mean age 66 ± 14 years) with unexplained syncope were randomized to "conventional" testing with an external loop recorder, tilt and electrophysiologic testing or immediate prolonged monitoring with an ILR with 1 year of monitoring. Patients were excluded if they had a left ventricular ejection fraction < 35%. Patients were offered crossover to the alternate strategy if they remained undiagnosed after their assigned strategy. A diagnosis was obtained in 14 of 27 patients randomized to prolonged monitoring, compared to 6 of 30 undergoing conventional testing (52 vs 20%, $p = 0.012$). Crossover was associated with a diagnosis in 1 of 6 patients undergoing conventional testing, compared to 8 of 13 patients who completed monitoring (17 vs 62%, $p = 0.069$). Overall, prolonged monitoring was more likely to result in a diagnosis than conventional testing (55 vs 19%, $p = 0.0014$). Bradycardia was detected in 14 patients undergoing monitoring, compared to 3 patients with conventional testing (40 vs 8%, $p = 0.005$). These data illustrate the limitations of conventional diagnostic techniques for detection of arrhythmia, particularly bradycardia. Although there is clear selection bias in the enrolment of patients referred to an electrophysiologist for work-up, this study suggests that conventional testing has modest utility in patients with preserved left ventricular function.

In Ashby et al.¹⁰ retrospective study, after a mean follow-up of 5.6 ± 5.7 months, symptoms reoccurred in 25 (52.1%) patients at a mean of 2.8 ± 2.1 months after insertion of an ILR. No further symptoms occurred in 23 (47.9%) patients. Of the 25 patients who had a symptom and recorded an event, an arrhythmia was seen in 10 (40%) patients. Seven patients had bradycardia; 4 with profound sinus bradycardia/sinus arrest, 1 with complete heart block, and 2 in association with the cardioinhibitory component of vasovagal syncope. Three patients had tachycardias; 2 with supraventricular tachycardia and 1 with atrial flutter. Fifteen (60%) of the 25

patients who activated their device due to syncope or pre-syncope were in sinus rhythm during the event. The ILR was effective in making a cardiological or non-cardiological diagnosis for unexplained syncope or pre-syncope in 52.1% of the patients.

The literature¹¹⁻¹³ clearly supports the use of the ILR in patients with recurrent unexplained syncope that have failed a non-invasive work-up and continue to have syncope. This represents a select group that has been referred for further testing, where ongoing symptoms are likely and a symptom rhythm correlation is a feasible goal. Widespread early use of the ILR is likely to reduce the diagnostic yield as the prevalence of arrhythmias falls supported by data from the RAST trial^{14,15}. The optimal patient for prolonged monitoring has frequent recurrent symptoms suspicious for arrhythmia. After clinical assessment including determination of left ventricular function, a decision must be made if the clinical presentation is potentially life-threatening. Primary and secondary prevention trials using implantable defibrillators support this practice. All reports using the ILR have suggested a low incidence of life-threatening arrhythmia or significant morbidity with a prolonged monitoring strategy. Conversely, there may be a low risk population where an ILR is not warranted. This would include patients without heart disease and a relatively low burden of syncope, in whom testing has a low yield and the diagnosis is almost certainly benign¹⁵⁻¹⁸.

Loop recorders have significantly improved the ability to obtain rhythm symptom correlation physiologic data during spontaneous symptoms in patients with unexplained syncope. The ILR is a particularly useful tool for investigating patients with recurrent unexplained syncope when non-invasive tests are negative. The clinician should consider early use of the ILR when an arrhythmia is suspected, focusing on patients with a heavy syncope burden that are likely to experience recurrence.

References

1. Brignole M, Alboni P, Benditt D, et al, for the Task Force on Syncope, European Society of Cardiology. Guidelines on management (diagnosis and treatment) of syncope. *Eur Heart J* 2001; 22: 1256-306.
2. Kurbaan AS, Franzen AC, Bowker TJ, et al. Usefulness of tilt test-induced patterns of heart rate and blood pressure using a two-stage protocol with glyceryl trinitrate provocation in patients with syncope of unknown origin. *Am J Cardiol* 1999; 84: 665-70.
3. Bloomfield D, Maurer M, Bigger Jr JT. Effects of age on outcome of tilt-table testing. *Am J Cardiol* 1999; 83: 1055-8.
4. Krahn AD, Klein GJ, Yee R, et al, for the REVEAL Investigators. Use of extended monitoring strategy in patients with problematic syncope. *Circulation* 1999; 99: 406-10.
5. Menozzi C, Brignole M, Garcia-Civera R, et al, for the International Study on Syncope of Uncertain Etiology (ISSUE) Investigators. Mechanism of syncope in patients with heart disease and negative electrophysiologic test. *Circulation* 2002; 105: 2741-5.

6. Moya A, Brignole M, Menozzi C, et al, for the 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: 1261-7.
7. Brignole M, Menozzi C, Moya A, et al, for the International Study on Syncope of Uncertain Etiology (ISSUE) Investigators. Mechanism of syncope in patients with bundle branch block and negative electrophysiological test. *Circulation* 2001; 104: 2045-50.
8. Moss AJ, Zareba W, Hall WJ, et al, for the Multicenter Automatic Defibrillator Implantation Trial II Investigators. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med* 2002; 346: 877-83.
9. Krahn AD, Klein GJ, Yee R, et al. Randomized Assessment of Syncope Trial: conventional diagnostic testing versus a prolonged monitoring strategy. *Circulation* 2001; 104: 46-51.
10. 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: 1200-5.
11. Nierop PR, van Mechelen R, van Elsacker A, et al. Heart rhythm during syncope and presyncope: results of implantable loop recorder. *Pacing Clin Electrophysiol* 2000; 23: 1532-8.
12. Seidl K, Rameken M, Breunung S, et al, on behalf of the REVEAL Investigators. Diagnostic assessment of recurrent unexplained syncope with a new subcutaneously implantable loop recorder. *Europace* 2000; 2: 256-62.
13. Sivakumaran S, Krahn AD, Klein GJ, et al. A prospective randomized comparison of loop recorders versus Holter monitors in patients with syncope or presyncope. *Am J Med* 2003; 115: 1-5.
14. Garcia-Civera R, Ruiz-Granell R, Morell-Cabedo S, et al. Selective use of diagnostic tests in patients with syncope of unknown cause. *J Am Coll Cardiol* 2003; 41: 787-90.
15. Benditt DG, Brignole M. Syncope: is a diagnosis a diagnosis? *J Am Coll Cardiol* 2003; 41: 791-4.
16. Mason PK, Wood MA, Reese DB, et al. Usefulness of implantable loop recorders in office-based practice for evaluation of syncope in patients with and without structural heart disease. *Am J Cardiol* 2003; 92: 1127-9.
17. Krahn AD, Klein GJ, Yee R, et al. Cost implications of testing strategy in patients with syncope: randomized assessment of syncope trial. *J Am Coll Cardiol* 2003; 42: 495-501.
18. Chrysostomakis SI, Klapsinos NC, Simantirakis EN, et al. Sensing issues related to the clinical use of implantable loop recorders. *Europace* 2003; 5: 143-8.