Implantable loop recorder: towards a gold standard for the diagnosis of syncope?

Syncope is a transient symptom and not a disease. Typically, patients are asymptomatic at the time of evaluation and the opportunity to capture a spontaneous event during diagnostic testing is rare. As a result, diagnostic evaluation has focused on the detection of abnormalities that could plausibly cause loss of consciousness. This type of reasoning necessarily leads to uncertainty in establishing a cause. In other words, the causal relation between an abnormality found during the diagnostic workup and syncope is often presumptive. Indeed, in the tests used to evaluate the aetiology of syncope, it is not possible to measure test sensitivity and specificity, owing to the lack of a reference standard for most of the tests. Because of the episodic behaviour of syncope, the opportunity of correlating the spontaneous syncopal episodes with an abnormal finding can be considered as a reference standard.

Role of the implantable loop recorder
An implantable ECG event monitor has recently become available (Reveal, Medtronic). This device is placed subcutaneously under local anaesthesia, and has a battery life of 15–18 months. The device has a solid state loop memory and, with the current version, the ECG of up to 40 minutes before and two minutes after activation can be stored. With these characteristics, if patients activate the device when consciousness has been restored, there is a high probability of having a correlation of ECG signals and syncope. In the first reported experience, the device was used in a heterogeneous population of 85 patients affected by unexplained syncope,1 which included patients with and without structural heart disease as well as patients with and without abnormalities in baseline ECG. Syncope-ECG correlation was achieved in 27% of patients and presyncope-ECG correlation in 32%; the rhythm recorded during the event was heterogeneous, thus reflecting the various clinical settings of the population enrolled: 29 patients were in sinus rhythm, three had supraventricular tachycardia, and 18 had some type of “bradyarrhythmia”, the origin of which was considered to be neurally mediated in seven patients. This study showed that patient activated, long term monitoring is feasible, helpful, safe, and probably cost effective.

From that initial experience it appeared that the implantable loop recorder might become the reference standard to be adopted when an arrhythmic cause of syncope is suspected but not sufficiently proven. There are several areas of interest:

- **Tilt induced vasovagal syncope**—We do not know whether the type of response induced during tilt testing (vasodepressor, mixed, cardioinhibitory) correlates with the spontaneous vasovagal attack. Knowing the exact mechanism of the spontaneous attack is of course of great practical importance in choosing the best treatment. One recent trial has shown that pacemaker therapy is highly efficacious in preventing syncopal recurrences in patients with cardioinhibitory vasovagal syncope. More generally, the same reasoning applies to all patients who have a likely diagnosis of neurally mediated syncope based on typical history (vasovagal syncope, situational syncope—that is, syncope that occurs during micturition, defaecation, swallowing or coughing—and carotid sinus syncope).

- **Isolated syncope**—This term can be applied to patients without apparent structural heart disease, normal ECG, and with a complete negative diagnostic work up, including tilt testing. In these patients there is a large consensus that the likely cause is neurally mediated.

- **Bundle branch block, negative electrophysiological study**—In these patients, progression to complete atrioventricular (AV) block occurs in about 20% of cases within a few years, despite a complete negative electrophysiologic evaluation.1,2

- **Severe left ventricular dysfunction, non-sustained ventricular tachyarrhythmias, and negative electrophysiological study**—We know, for example, from the MUSTT (multi-centre unsustained tachycardia trial) registry,3 that these patients have a lower risk of sudden death or arrhythmic events than those with a positive electrophysiologic study, but their risk still remains unacceptably high, being 24% and 32% at five years, respectively.

- **Adenosine sensitive syncope**—Some patients with unexplained syncope show an increased susceptibility to intravenous injection of adenosine or adenosine triphosphate (ATP), which results in a prolonged asystolic pause caused by paroxysmal AV block.6,7 The logical inference is that ATP testing can identify patients with syncope caused by transient AV block even when the electrophysiologic findings and other conventional tests are unremarkable. However, this remains a hypothesis to be confirmed by prospective studies aimed at demonstrating a similar abnormality during the spontaneous syncope.

The early lessons we are learning: the implantable loop recorder in “isolated” syncope and tilt positive syncope
ISSUE (international study on syncope of uncertain etiology) is an ongoing prospective study which aims to analyse the diagnostic yield of the implantable loop recorder in specific subgroups of patients with syncope of uncertain aetiology; the groups were predefined and the patients assigned to their groups at the time of enrolment.8 Overall, more than 200 patients have been enrolled and are being followed up. To date, we have only preliminary results on the subgroup of patients with isolated syncope (that is, no heart disease and complete negative work up including tilt testing) and on the subgroup of patients with positive response to tilt testing and no heart disease. The main findings are the following:

- In both groups, about two thirds of patients had no recurrence during follow up; of those who had recurrences, no patients suffered trauma or consequences caused by syncope. The low recurrence rate and the low risk of related injury we observed in the “real
In the tilt positive patients, the results were very similar among the patients with isolated syncope who had sinus pause of 4 seconds. Time of syncope shows a progressive sinus bradycardia with a maximum severe bradycardia lasting two minutes. (B) The expanded ECG at the time of syncope shows an 8.5 second asystolic pause caused by AV block which coincides with a pronounced sinus rate slowing. The association, at the same time, of sinus bradycardia and AV block strongly suggests that a vagal reflex is the mechanism responsible for the event.

Concerns about the use of the implantable loop recorder

Apart from research purposes, ultimately the implantable loop recorder is used to find the most appropriate treatment of arrhythmias which cause syncope. Therefore, its use should be limited to patients with a high probability of arrhythmic syncope in whom the severity, frequency or hazardous nature of the episodes warrants specific treatment.

A diagnosis should be considered established only when syncope episodes can be detected; in this case, the test can be regarded as the “gold standard”. The recording of presyncope or asymptomatic arrhythmia—which is feasible in the new automatic, computerized version of the device—leaves the diagnosis uncertain.

Although the documentation of bradycardia concurrent with a syncope episode is considered diagnostic, further evaluations may nevertheless be necessary in order to discriminate between an intrinsic cardiogenic abnormality and a neurogenic mechanism. Moreover, in the case of patient with the recording of a cardioinhibitory neurally mediated syncope, one cannot exclude the possibility that the patient may also have different episodes—that is, vasodepressor.

Disadvantages of the implantable loop recorder include the need to implant an instrument in the patient, the lack of recording of any other concurrent physiological parameter (for example, blood pressure), and the high cost of the implantable device.

On the behalf of the International Study on Syncope of Uncertain Etiology (ISSUE) Investigators

Michele Brignole

Department of Cardiology and Arrhythmologic Centre, Ospedali Riuniti, Lavagna, Italy

Carlo Menozzi

Department of Cardiology, Unit of Interventional Cardiology, Ospedale S Maria Nuova, Reggio Emilia, Italy

Angel Moya

Unitat d’Aritmies, Department of Cardiology, Hospital General Vall d’Hebron, Barcelona, Spain

Roberto Garcia-Civera

Servicio de Cardiologia, Hospital Clinico, Valencia, Spain

On June 11, 2022 by guest. Protected by copyright.
IMAGES IN CARDIOLOGY

Improvement in the pulmonary circulation following pulmonary thromboendarterectomy

Chronic pulmonary thromboembolic disease is an insidious, life threatening condition that develops as a long term complication of the incomplete resolution of pulmonary embolism. Patients present with progressive breathlessness on exertion and the prognosis is poor owing to the development of pulmonary hypertension, with less than 30% five year survival. Pulmonary thromboendarterectomy has emerged as an effective treatment in selected patients.

Our patient was a 64 year old man with a five year history of progressive dyspnoea on effort following documented pulmonary embolism. He presented with severe exercise limitation (New York Heart Association functional class III) and signs of right ventricular hypertrophy. Invasive studies revealed a mean pulmonary arterial pressure of 65 mm Hg and a cardiac index of 2.06 l/min/m². Contrast enhanced three dimensional magnetic resonance angiography (MRA) (below left) confirmed pulmonary thromboembolic disease with multiple abrupt occlusions of segmental pulmonary arterial branches in both lower lobes and in the right upper lobe (arrows), proximal arterial dilatation, and vessel tortuosity. Pulmonary thromboendarterectomy was carried out under hypothermic circulatory arrest and an extensive cast of organised clot and thrombus was removed from the pulmonary arterial tree. The patient has made an uneventful recovery and at three months after surgery is asymptomatic, walking up to three miles daily. Mean pulmonary arterial pressure has fallen to 22 mm Hg and the cardiac index has improved (2.92 l/min/m²). Repeat MRA demonstrates dramatic improvement in the pulmonary circulation with enhanced blood flow detected in subsegmental pulmonary arterial branches and in the pulmonary veins (below right).

RANA SAYEED
RICHARD COULDEN
JOHN DUNNING