Original article

High incidence of tachyarrhythmias detected by an implantable loop recorder in patients with unexplained syncope

Christiana Schernthaner, Franz Danmayr, Johann Altenberger, Maximilian Pichler, Bernhard Strohmer

Department of Cardiology, Salzburger Landeskliniken, Paracelsus Private Medical University, Salzburg, Austria

Abstract

Background: Syncope is a complex clinical syndrome that may be challenging with respect to a definite diagnosis. The implantable loop recorder (ILR) is a useful tool to define but also to exclude an arrhythmic aetiology.

Aim: To investigate the causes of recurrent syncope or near-syncope with respect to underlying arrhythmias in non-selected consecutive patients monitored with an ILR.

Methods: A retrospective study was conducted including 55 patients (34 men, 21 women; age 60±19 years) with unexplained syncope who received an ILR for prolonged monitoring at our institution between April 1998 and October 2006.

Results: Forty (73%) patients had a recurrence of syncope or near-syncope. Structural heart disease was present in 18 (33%) patients, 4 of them having an ejection fraction <35%. An arrhythmia was detected as the cause of syncope in 25 (46%) patients. The ILR was successful in establishing a symptom-rhythm correlation in 63%. The mean follow-up period from implantation to occurrence of the detected arrhythmias was 9±8 months. Bradyarrhythmias were recorded in 12 (22%) patients, whereas tachyarrhythmias were found in 13 (24%) patients. Narrow QRS tachycardia was the underlying arrhythmia in 6 patients and wide QRS tachycardia in 7 patients. A pacemaker was implanted in all 12 patients with bradyarrhythmias. Implantable cardioverter defibrillator (ICD) therapy was indicated in 6 patients with adjunctive catheter ablation in 3 of them. Four patients presenting with paroxysmal supraventricular tachycardia were treated with radiofrequency catheter ablation.

Conclusion: The ILR helped efficaciously to determine the correct diagnosis and appropriate treatment of recurrent syncope. A considerably high proportion of tachyarrhythmias was detected in this non-selected consecutive population. The majority of patients with tachyarrhythmic syncope required defibrillator implantation and/or radiofrequency ablation.

Key words: syncope, implantable loop recorder, tachyarrhythmia

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Introduction

Syncope is a complex clinical syndrome that can be very challenging with respect to a definite diagnosis. The implantable loop recorder (ILR) is a useful tool to define but also to exclude an arrhythmic aetiology. According to the recent guidelines of the European Society of Cardiology the implantation of an ILR is indicated in patients who have clinical or electrocardiographic features suggesting an arrhythmic syncope when the mechanism of syncope remains unclear (Class I) [1]. The purpose of this study was to investigate the causes of recurrent syncope or near-syncope with respect to underlying arrhythmias in non-selected consecutive patients monitored with an ILR [2].

Methods

Study design

We retrospectively analysed the causes of syncope or near-syncope of 55 patients (34 men, 21 women; mean age 60±19 years) who received an ILR (Reveal® 9525 and Reveal Plus® 9526, Medtronic, Minneapolis, MN, USA) at our institution between April 1998 and October 2006 because of two or more unexplained episodes of syncope in the last two years. Prior to implantation all patients

Address for correspondence:
Christiana Schernthaner MD, Paracelsus Private Medical University, Salzburger Landeskliniken, St. Johanns-Spital, Department of Cardiology, Muellner Hauptstrasse 48, A-5020 Salzburg, Austria, tel.: +43 662 4482 3481, fax: +43 662 4482 3486, e-mail: c.schernthaner@tele2.at

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underwent neurological work-up including neurological status and electroencephalogram. The cardiac investigations comprised a 12-lead ECG at rest, 24-hour Holter monitoring, a transthoracic echocardiogram, an exercise stress test, carotid sinus massage and tilt table testing. Patients were referred for invasive diagnostic catheter procedures, such as coronary angiography or electrophysiological study, at the discretion of the responsible physician.

Study procedure

All patients gave their written informed consent prior to implantation of the ILR. Pre-implant surface mapping with standard ECG electrodes was performed in order to achieve a good signal quality. All devices were implanted subcutaneously in the left pectoral or precordial region using local anaesthesia. The ILR was programmed the day after implantation, focussing on optimal sensitivity and gain settings. According to our protocol the parameters for auto-activation of event recording were set to pauses ≥3 seconds of asystole, a heart rate ≤30 beats per minute (bpm) or a heart rate ≥145 bpm. The ECG storage capacity was programmed to store three auto-activated events and the last five patient-activated events. All patients underwent detailed training on how to correctly handle the activator device. Furthermore, patients and their family members were advised to read the instruction manual carefully. Ten days after implantation the patients were scheduled for the interrogation of a stored 'test event' in our outpatient clinic. Follow-up visits were scheduled regularly in 3 to 6-month intervals at our outpatient clinic including interrogation and analysis of the stored events. The minimum follow-up period for this study was 1 month. In case of a syncopal event, device interrogation was performed within the following 24 hours.

Table I. Clinical characteristics of the study population (total number N=55)

Variable	Value
Age [years]	60±19
Male gender	34 (62%)
Structural heart disease	18 (33%)
Coronary artery disease	16 (29%)
Left ventricular ejection fraction (LVEF) [%]	54±9
LVEF ≤35%	4 (7%)
Left ventricular end-diastolic dimension [mm]	51±7
Heart rate [beats per minutes]	74±14
QRS duration [ms]	107±25
bundle branch block	4 (7%)
Atrial fibrillation	16 (29%)
permanent	5 (9%)
paroxysmal	11 (20%)

Statistical analysis

Analyses were performed using the statistical software program Excel Microsoft. Characteristics of subjects are presented as means and standard deviations or number and percentage, if nothing else is indicated.

Results

Patient characteristics

The baseline characteristics of the patients are shown in Table I. Structural heart disease was present in 18 (33%) patients. Ischaemic cardiomyopathy was found in 3 (5%), idiopathic dilated cardiomyopathy in 4 (7%) and valvular cardiomyopathy in 2 (4%) patients. Coronary artery disease diagnosed by angiography was present in 16 (29%) patients. Recipients of the ILR had a mean LV ejection fraction (LVEF) of 54±9%. However, four patients with cardiomyopathy had an LVEF ≤35%. The underlying rhythm at baseline was sinus rhythm in 39 (71%) patients and atrial fibrillation (AF) in 16 (29%) patients. Permanent AF was present in 5 (9%) patients, whereas 11 (20%) patients had a history of documented paroxysmal AF. The mean QRS duration was 107±25 milliseconds (ms). A pre-

Table II. Clinical diagnosis, treatment based on cardiac rhythm during recurrent syncope

Variable	Value	Therapy
Syncope of any cause	40 (73%)	
Syncope due to arrhythmias	25 (46%)	
Bradyarrhythmias	12 (22%)	
sinus bradycardia <30 beats/min	3	PM (n=3)
sinus pause ≥4 s	4	PM (n=4)
paroxysmal heart block	5	PM (n=5)
Tachyarrhythmias	13 (24%)	
paroxysmal supraventricular tachycardia	6	RFA (n=4),
		AAD (n=2)
ventricular tachycardia	6	ICD (n=5),
		RFA (n=3),
		AAD (n=1)
torsade de pointes	1	ICD + RFA
Syncope without documented arrhythmia	15 (27%)	
neurally mediated syncope	3	tilt training
coughing	1	no therapy
epilepsy	2	drugs
drop attack	1	drugs
Munchausen syndrome	1	psychiatric referral
duodenal ulcer	1	drug therapy
unexplained	6	no therapy

Abbreviations: PM – pacemaker, RFA – radiofrequency catheter ablation, AAD – anti-arrhythmic drug therapy, ICD – implantable cardioverter-defibrillator

-existing bundle branch block pattern was found on surface ECG in 4 patients. Coronary artery disease was diagnosed in 18 of the 27 patients undergoing invasive coronary angiography. An electrophysiological study was performed prior to ILR implantation in 20 patients, but failed to establish a definite diagnosis in 19 of them. In one patient, however, two different forms of supraventricular tachycardia were induced and ablated successfully before implantation of the ILR. All patients showed a negative head-up tilt table test, a negative carotid sinus massage and an unremarkable neurological workup in addition.

Symptom-Arrhythmia Correlation

Recurrence of syncope or near-syncope of any cause occurred in 40 (73%) patients. The results and treatment approaches in these patients are summarised in Table II. The mean time from implantation to the recurrent clinical event was 7.6±6.6 months (range 1-21). Arrhythmias were detected as the cause of the recurrent event in 25 (46%) patients. Thus, the ILR was successful in establishing a symptom-arrhythmia correlation in 63%. The mean time from implantation to the recorded first arrhythmic event was 9.2±8.4 months (range 1-27). In 12 patients (22%) interrogation of the ILR revealed bradyarrhythmias, such as sick sinus syndrome with bradycardia in 3 and significant pauses in 4 patients and a paroxysmal high--grade AV block in 5 patients. A pacemaker was implanted in all 12 patients with documented and symptomatic bradyarrhythmias.

Primary tachyarrhythmias were documented by the ILR at the time of syncope in 13 (24%) patients. Narrow QRS tachycardia was recorded in 6 patients and wide QRS tachycardia in 7 patients. Four of the 6 patients presenting with syncopal paroxysmal supraventricular tachycardia underwent an electrophysiological study, whereas one young patient refused to undergo the invasive procedure. Typical atrioventricular nodal re-entrant tachycardias were diagnosed in 3 patients, one of them presenting in combination with atrial flutter. Atrioventricular re-entrant tachycardia related to a right posteroseptal accessory pathway was found in one patient (Figure 1). All arrhythmias including the typical atrial flutter were treated successfully with radiofrequency catheter

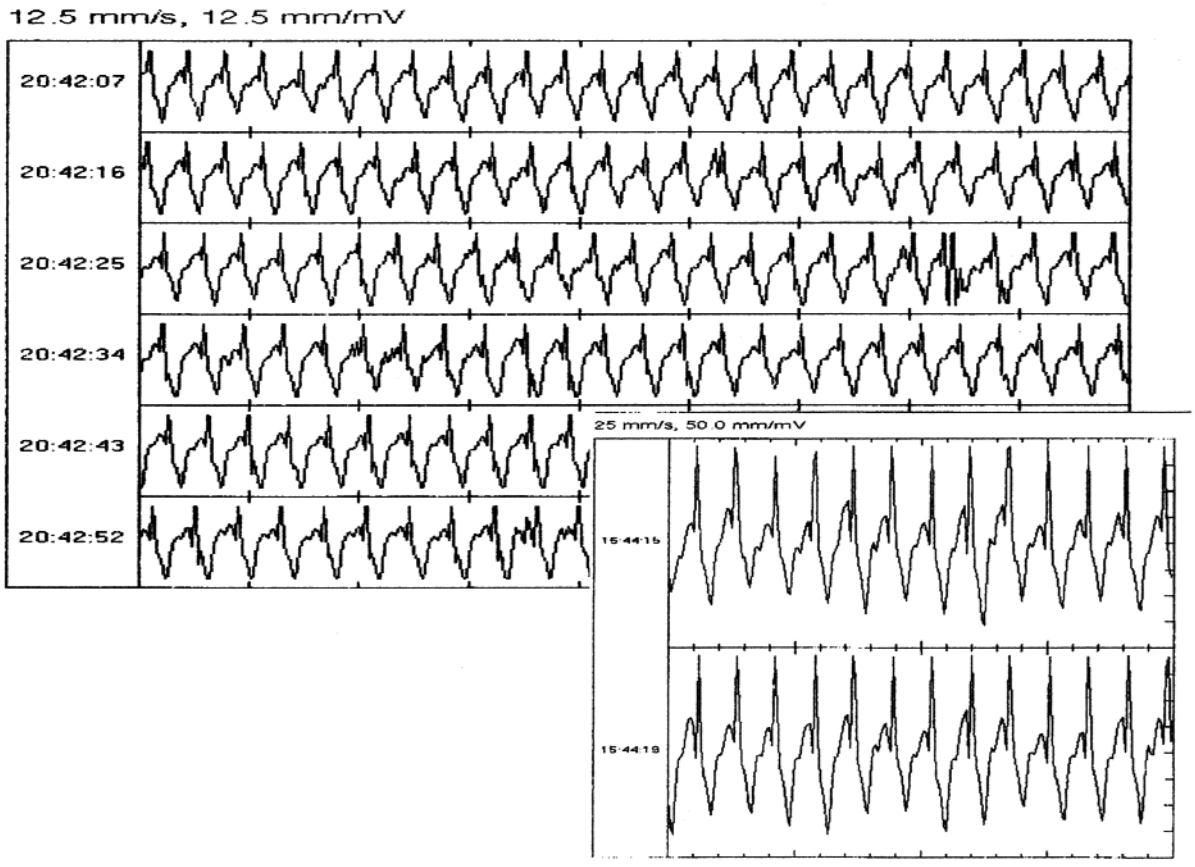

Figure 1. A narrow QRS complex tachycardia with a cycle length of 300 ms was stored by the implantable loop recorder (ILR) during a syncopal event in a healthy 33-year-old man. The patient was referred for an electrophysiological study. Atrioventricular reentrant tachycardia using a right posteroseptal accessory pathway was diagnosed and ablated successfully at the same session

ablation. One patient underwent an electroanatomically--guided circumferential ablation of all four pulmonary veins for treatment of the documented paroxysmal AF. Another patient with symptomatic paroxysmal AF was treated with a class I antiarrhythmic drug.

Wide QRS complex tachycardia was indicative of ventricular tachycardia in 6 patients, and of torsade de pointes in one patient. Five of the 6 patients had reduced left ventricular (LV) function, 4 patients were diagnosed to have a non-ischaemic cardiomyopathy (LVEF 27±3%), and one patient an ischaemic cardiomyopathy with postero-basal wall motion abnormality, whereas the other 2 patients showed preserved LV function. A cardioverter-defibrillator (ICD) was implanted in 6 patients for treatment of syncopal ventricular tachycardia and idiopathic ventricular fibrillation (Table II). In addition, adjunctive radiofrequency catheter ablation was performed in 3 of these patients for prevention of frequent ICD discharges. The substrates for ablation were focal ventricular tachycardia, bundle branch re-entrant tachycardia (Figure 2) related to non-ischaemic dilated cardiomyopathy and malignant Purkinje extrasystole in a structurally normal heart. One patient with documented rapid AF triggering non-sustained ventricular tachycardia was treated with amiodarone (Figure 3).

In 15 (27%) patients an arrhythmia was excluded with high probability as the explanation for recurrent syncope or near-syncope. Neurally mediated syncope was considered to be the mechanism in 3 patients who demonstrated no detectable changes in heart rate during the syncopal event (vasodepressor type 3). Repeated tilt table testing with additional application of nitro-glycerine confirmed the diagnosis. Further investigations revealed causes or circumstances for syncope among the other individuals, such as epilepsy in 2 patients, syncope due to excessive coughing in 1 patient, drop attacks in 1 patient and Munchausen syndrome in 1 patient. Another patient, who suffered recurrent postprandial syncope, was diagnosed with a *Helicobacter pylori*-positive duodenal ulcer. The causes for syncope occurring in the absence of documented arrhythmias in the ILR could not be clarified definitely in the remaining 6 patients.

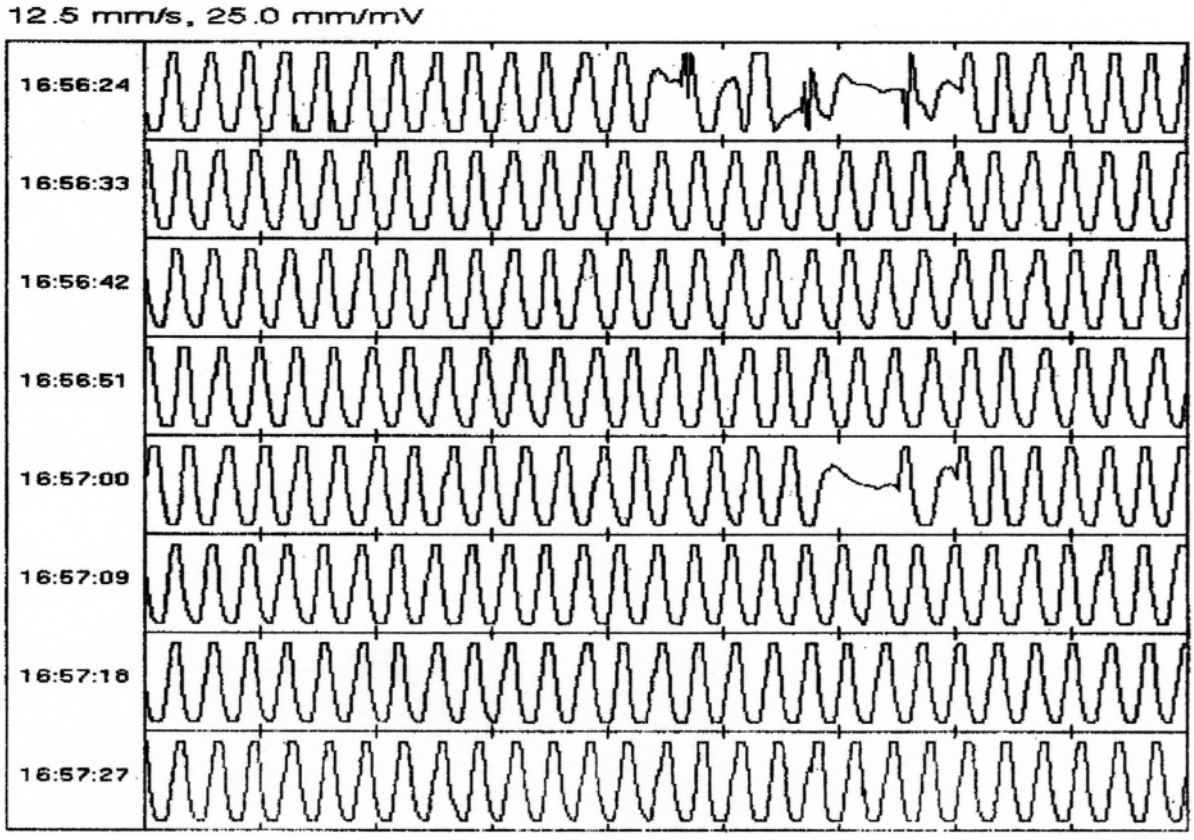

Figure 2. Wide QRS complex tachycardia recorded by the ILR during syncope in a 66-year-old woman with non--ischaemic cardiomyopathy and reduced pump function. The electrocardiographic recording shows a monomorphic ventricular tachycardia at a cycle length of 300 ms with spontaneous onset and termination. The electrophysiological study demonstrated a bundle brunch reentrant tachycardia as the underlying mechanism and was treated successfully with radiofrequency catheter ablation. In addition, an implantable cardioverter defibrillator (ICD) was inserted prophylactically because of the diseased heart

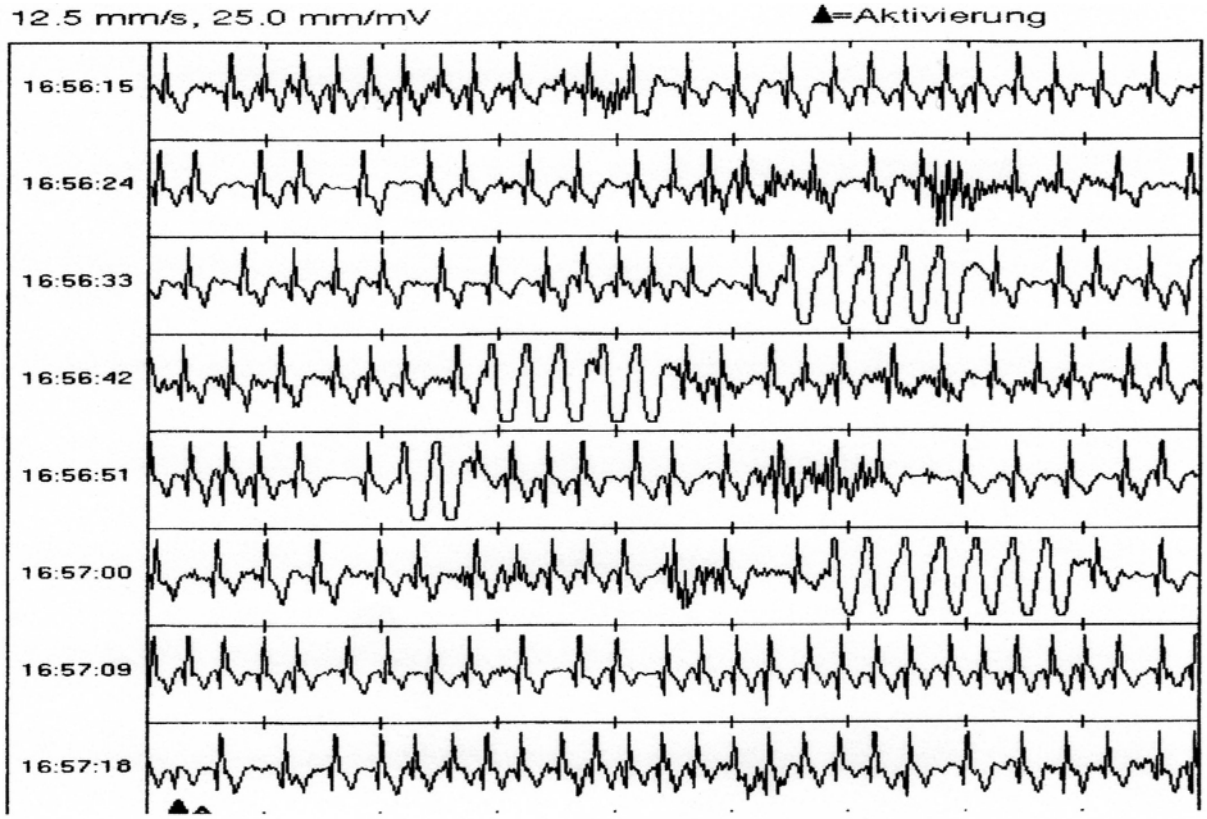

Figure 3. The ILR registration that was activated by a 53-year-old man without significant structural heart disease (small black triangle below the bottom ECG line) immediately before a near-syncopal event in a stressful working environment. The tracing shows rapid atrial fibrillation interrupted by non-sustained ventricular tachycardia. Based on this information the patient was treated with amiodarone for rhythm and rate control of paroxysmal atrial fibrillation

Discussion

Although the mechanism of syncope was heterogeneous in this study, an arrhythmia was detected as the cause of the recurrent event in about half of the patients. The ILR was successful in establishing a symptom-rhythm correlation in 25 (63%) of the 40 patients. The most important finding, however, is the relative high incidence of tachyarrhythmias, accounting for one-half of the recorded syncopal arrhythmias. Interestingly, the distribution between supraventricular und ventricular tachycardias was balanced in our series. The majority of patients with ventricular tachycardia were characterised by overt heart disease and reduced LV function.

Our findings deserve consideration for the management of patients presenting with unexplained syncope or near-syncope in clinical practice. In fact, awareness of this problem has only partly surfaced in the literature dealing with prolonged monitoring using an ILR. Solano et al. reported in their prospective study including two hospitals only 2/106 patients, who demonstrated ventricular tachycardia based on structural heart disease during a median follow-up of 13 months [3]. Boersma et al. as well as Mason et al. reported only one ventricular tachycardia in each of their series of 43 patients monitored with an ILR for a median time of 18 and 11 months, respectively [4, 5]. The investigators of the International Study on Syncope of Uncertain Etiology (ISSUE) applied an ILR to 35 patients with overt structural heart disease and high risk of ventricular arrhythmias, in whom the electrophysiological study was unremarkable [6]. Syncope recurred in only 6 patients after a mean follow-up period of 6 months, and sustained ventricular tachycardia was detected in only one patient. The authors of this study argued therefore that structural heart disease and syncope do not automatically equate to ventricular arrhythmias and high mortality. In contrast to that, Knight et al. conducted a small prospective study including 14 patients with non-ischaemic cardiomyopathy, unexplained syncope and a negative electrophysiology test [7]. They found that recurrent syncope of patients monitored and treated with an ICD over a mean period of 24 months was always associated with ventricular tachyarrhythmias.

Invasive electrophysiological study has a limited yield in the evaluation of syncope in patients with no cardiac

history but also in patients with cardiac history [8, 9]. Despite the potential malignancy of the documented tachyarrhythmias, none of the patients in the present study experienced a severe injury or poor outcome. However, it is noteworthy that a 40-year old patient diagnosed with malignant His-Purkinje extrasystole suffered a near-agonal state during prolonged torsade de pointes [10]. It is noteworthy that none of the patients with unexplained syncope met definite criteria for prophylactic implantation of an ICD at the time of the initial clinical evaluation. Within the last few years, however, indications for prophylactic implantation of an ICD have been expanded and implemented into the recent guidelines [11]. In our opinion, the ILR may be helpful for the evaluation of patients with unexplained syncope, particularly in the presence of structural heart disease, such as previous myocardial infarction or idiopathic cardiomyopathy, but only moderately reduced LV function [12]. Furthermore, the newer generation of ILR with extended longevity may help to monitor patients with electrical disorders of the heart, for instance the Brugada syndrome, whenever such patients are characterised by low to intermediate risk and prophylactic device therapy is refused by the patient due to a lack of rhythm-symptom correlation [13].

It is well known that occurrences of paroxysmal supraventricular tachycardia infrequently lead to syncope [14]. A large prospective multicentre trial (ISSUE 2) evaluated the diagnostic and therapeutic value of the ILR in a total of 392 patients with recurrent suspected neurally mediated syncope [15]. After a median of 3 months syncope was documented by the ILR in 106 (26%) patients, more than half of these patients having prolonged asystolic pauses. Only a minority of patients (8%) showed primary tachyarrhythmias, such as paroxysmal AF in 3, paroxysmal supraventricular tachycardia in 5 and ventricular tachycardia in 1 patient. Similar to that, Krahn et al. and Nierop et al. observed tachyarrhythmic events underlying syncope in 4-11% of cases, respectively [16, 17].

An underestimated cause of syncope might be related to the concept of tachycardia-induced tachycardia. The clinician has to be aware that very rapid supraventricular tachyarrhythmias may potentially induce cardiovascular collapse or even degenerate into life-threatening ventricular arrhythmias [18, 19]. Apart from the Wolff-Parkinson-White syndrome, typically patients with advanced heart disease are prone to develop these complications. However, we were able to document a pre-syncope related to the above-mentioned concept in a patient without significant heart disease but rapidly conducting AF interrupted by non-sustained runs of ventricular tachycardia during strenuous work in a bakery (Figure 3).

In line with previous results the present study demonstrated that early application of an ILR is a helpful and safe strategy for patients with unexplained syncope after a basic clinical work-up. In nearly half of the patients specific device and/or ablational therapy was initiated based on the ECG documentation by the ILR, preventing further recurrences of syncope and hospitalisations [20].

Limitations

Some limitations must be taken into account when interpreting the results of this observational study. First, the study was conducted retrospectively comprising a relatively small number of non-selected patients. In some cases the follow-up time may not have been adequate to establish the diagnosis. Secondly, the yield of the ILR in providing a definite diagnosis may differ from previous studies related to variations in patient selection and screening modalities prior to implantation of the loop recorder. The high prevalence of tachyarrhythmias detected by continuous monitoring in the present report might be explained in part by the lack of an electrophysiological study prior to the ILR implantation. In general, electrophysiological testing is indicated in syncopal patients with depressed systolic function as inducibility of sustained ventricular tachycardia can predict a life-threatening arrhythmic syncope and has a considerable impact on the selection of therapy.

Conclusion

ILR technology was useful to establish a symptom--rhythm correlation in about two thirds of the patients presenting with unexplained syncope. As a novel finding a relatively high proportion of tachyarrhythmias were detected as the cause of recurrent events. Based on this information specific interventions, such as defibrillator therapy and catheter ablation, were indicated for treatment or prevention of further potentially harmful events. In conclusion, the ILR has been proven to be a safe and effective way for characterisation of arrhythmogenic syncope, particularly if symptoms are recurrent but too infrequent for conventional monitoring techniques.

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Wysoka częstość wykrywania tachyarytmii za pomocą wszczepialnego rejestratora arytmii u chorych z niewyjaśnionym omdleniem

Christiana Schernthaner, Franz Danmayr, Johann Altenberger, Maximilian Pichler, Bernhard Strohmer

Department of Cardiology, Salzburger Landeskliniken, Paracelsus Private Medical University, Salzburg, Austria

Streszczenie

Wstęp: Omdlenie jest złożonym zespołem klinicznym, a wykrycie przyczyny utrat przytomności może być trudne. Implantowany pętlowy rejestrator arytmii (ILR) jest użytecznym narzędziem do potwierdzenia lub wykluczenia arytmii serca jako przyczyny omdlenia.

Cel: Ustalenie przyczyny omdleń lub stanów przedomdleniowych za pomocą rejestracji EKG urządzeniem ILR w grupie kolejnych chorych.

Metodyka: Retrospektywne badanie objęło 55 chorych (34 mężczyzn, 21 kobiet, średni wiek 60±19 lat) z niewyjaśnionym omdleniem, u których w naszej klinice implantowano ILR pomiędzy kwietniem 1998 a październikiem 2006 r.

Wyniki: Nawrót omdlenia lub stanu przedomdleniowego wystąpił u 40 (73%) chorych. Organiczną chorobę serca stwierdzono u 18 (33%) chorych, spośród których 4 miało frakcję wyrzutową lewej komory <35%. Arytmię jako przyczynę omdlenia wykryto za pomocą ILR u 25 (46%) chorych. Urządzenie okazało się skuteczne w ustalaniu korelacji objawów z rytmem serca u 63% chorych. Średni czas obserwacji od momentu implantacji do wystąpienia arytmii odpowiedzialnej za omdlenie wynosił 9±8 mies. Bradyarytmie zanotowano u 12 (22%) chorych, podczas gdy tachyarytmia była przyczyną omdlenia u 13 (24%) chorych, z tego u 6 był to częstoskurcz z wąskimi zespołami QRS, zaś u pozostałych 7 – z szerokimi zespołami QRS. U wszystkich 12 chorych z bradyarytmią wszczepiono układ stymulujący. U 6 innych chorych implantowano automatyczny kardiowerter-defibrylator, u 3 z nich wykonano również ablację.

Wnioski: Urządzenie ILR pomogło w ustaleniu przyczyny omdlenia i wdrożeniu odpowiedniego leczenia u większości chorych z grupy badanej. W omawianej populacji obserwowano wysoki odsetek tachyarytmii jako przyczyny omdlenia, a większość z tych chorych wymagała wszczepienia kardiowertera-defibrylatora i/lub ablacji.

Słowa kluczowe: omdlenie, implantowany pętlowy rejestrator EKG, tachyarytmia

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Adres do korespondencji:

Christiana Schernthaner MD, Paracelsus Private Medical University, Salzburger Landeskliniken, St. Johanns-Spital, Department of Cardiology, Muellner Hauptstrasse 48, A-5020 Salzburg, Austria, tel.: +43 662 4482 3481, faks: +43 662 4482 3486, e-mail: c.schernthaner@tele2.at

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