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***Background*—**Because of its episodic behavior, the correlation of spontaneous syncope with an abnormal finding can be considered a reference standard.

Methods and Results—We inserted an implantable loop recorder in 111 patients with syncope, absence of significant structural heart disease, and a normal ECG; tilt-testing was negative in 82 (isolated syncope) and positive in 29 (tilt-positive). The patients had had ≥3 episodes of syncope in the previous 2 years and were followed up for 3 to 15 months. Results were similar in the isolated syncope group and the tilt-positive group: syncope recurred in 28 (34%) and 10 patients (34%), respectively, and electrocardiographic correlation was found in 24 (23%) and 8 (28%) patients, respectively. The most frequent finding, which was recorded in 46% and 62% of patients, respectively, was one or more prolonged asystolic pauses, mainly due to sinus arrest, preceded for a few minutes by progressive bradycardia or progressive tachycardia-bradycardia. Bradycardia without pauses was observed in 8% and 12% of cases, respectively. The remaining patients had normal sinus rhythm or sinus tachycardia, except for one, who had ectopic atrial tachycardia. In the tilt-positive group, an asystolic syncope was also recorded when the type of response to tilt-testing was vasodepressor or mixed. Presyncopal episodes were never characterized by asystolic pauses; normal sinus rhythm was the most frequent finding.

Conclusions—Homogeneous findings were observed during syncope. In most patients, the likely cause was neurally-mediated, and the most frequent mechanism was a bradycardic reflex. In the other cases, a normal sinus rhythm was frequently recorded. Presyncope was not an accurate surrogate for syncope in establishing a diagnosis. **(*Circulation*. 2001;104:1261-1267.)**

Key Words: syncope ■ arrhythmia ■ diagnosis ■ electrocardiography

Because of the episodic behavior of syncope, the correlation of spontaneous syncopal episodes with an abnormal finding can be regarded as a reference standard. An implantable ECG event monitor has recently become available, and it has been validated in patients with unexplained syncope.[1] This implantable loop recorder (ILR) is placed subcutaneously under local anesthesia, and it has a battery life of 15 to 18 months. The device has a solid-state loop memory, and the ECG for up to 40 minutes before and 2 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 correlating the electrocardiographic signal with the syncope.

In the present study, we implanted an ILR in patients with isolated syncope and in patients with tilt-positive syncope to obtain further information on the mechanism of syncope and to evaluate the natural history of these patients.

Methods

The International Study of Syncope of Uncertain Etiology (ISSUE) is a multicenter international prospective study aimed at analyzing the diagnostic contribution of an ILR in 4 predefined groups of patients with syncope of uncertain origin. (1) The isolated syncope group included patients without structural heart disease or with minor cardiac abnormalities that were considered to be without clinical relevance and not suggestive of a cardiac cause of syncope, absence of intraventricular conduction defects, and a negative complete work-up including tilt-testing. (2) The tilt-positive group included patients with the same characteristics as those in the isolated syncope group but who had a positive response to tilt-testing. (3) The suspected bradycardia group included patients with bundle-branch block and a negative electrophysiological test. (4) The

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*A complete list of Investigators appears in Appendix.

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TABLE 1. Patient Characteristics

	Isolated (n=82)	Tilt-Positive (n=29)
Age, y	63±17	64±15
Male sex, n (%)	45 (55)	11 (38)
History of syncope		
Duration, y (range)	4 (2–6)	3 (2–10)
No. (range) of episodes during last 2 years	4 (3–6)	3 (2–10)
Patients with presyncopal episodes during the last 2 years, n (%)	45 (55)	18 (62)
Severe trauma (wounds, fractures), n (%)	23 (28)	6 (21)
No warnings, n (%)	57 (76)	19 (66)
Vasoactive therapy at the time of the index syncope, n (%)	34 (41)	17 (59)
Standard electrocardiogram		
Any abnormality, n (%)	21 (26)	7 (24)
Echocardiogram		
Any abnormality, n (%)	21 (26)	7 (24)
Associated structural heart disease		
Any abnormality, n (%)	26 (32)	9 (31)
Ischemic	7	4
Valvular	5	1
Hypertensive	12	4
Other	2	0
Associated arrhythmias, n (%)		
Nonsustained ventricular tachycardia on Holter recording	3 (4)	3 (10)
Paroxysmal atrial fibrillation	2 (2)	3 (3)
Electrophysiological study performed, n (%)	61 (74)*	12 (41)*
Tilt-testing response		
Positive during the passive phase, n (%)	0	6 (21)
Positive during the drug phase, n (%)	0	23 (79)†
Asystolic response, n (%)	0	6 (21)
Maximum pause duration, s	0	10±5
Mixed type, n (%)	0	14 (48)
Vasodepressor type, n (%)	0	9 (31)

Values are mean±SD, median (range), or number of patients (percent).
*P=0.002.
†Challenge was by nitroglycerin in 21 and isoproterenol in 2 patients.

suspected tachycardia group included patients with overt heart disease who were at risk of ventricular arrhythmia, because these were patients with previous myocardial infarction or cardiomyopathy with depressed ejection fraction or nonsustained ventricular tachycardia in whom an electrophysiological study did not induce sustained ventricular arrhythmias.

The results reported here are those of the patients in the first 2 groups.

Study Protocol

Patients were considered eligible if they had had ≥3 syncopal episodes in the previous 2 years with an interval between the first and the last episode of >6 months. Patients were included in the study only if a careful history, physical examination, baseline ECG, carotid sinus massage, echocardiogram, and 24-hour ambulatory monitoring were not diagnostic of the cause of syncope. Any other test necessary for a definitive diagnosis of the cause of the syncope was performed when clinically indicated. In particular, an electrophysiological study was performed in patients with cardiac abnormalities or history of palpitations.

All patients underwent tilt-testing. The tilt-test protocol always included a baseline phase without drugs. A second phase with drug provocation, as well as the selection of intravenous isoproterenol or sublingual nitroglycerin, was performed according to the local protocol in each hospital.

When patients were deemed eligible, an ILR (Reveal, Medtronic) was implanted subcutaneously. The recommended programmed mode was 1 event, 21-minute preactivation, and 1-minute postactivation. Patients were instructed to activate the device after every episode of syncope or presyncope. The records of all episodes were retrieved, printed, and analyzed by investigators in each center and reevaluated by the 3 members of the Event Committee.

End Points

The primary end point of this study was the analysis of the electrocardiographic tracing obtained during the first syncopal episode that was correctly recorded by the device. Secondary end points were the study of the natural history of the patients and the analysis of electrocardiographic recordings when the device was activated for nonsyncopal episodes.

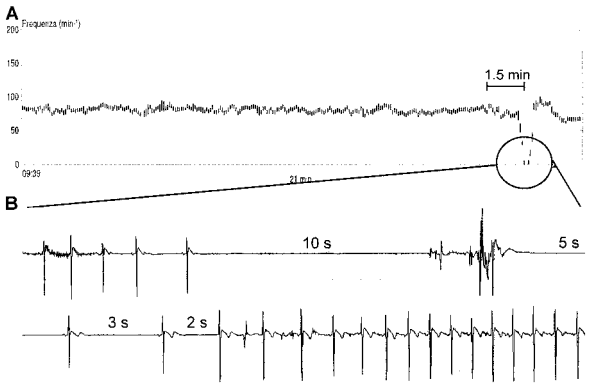

Figure 1. Patient with isolated syncope. A, Heart rate trend during 21 minutes of loop recording. Initially, heart rate is stable at ≈80 bpm; before syncope, there is a progressive mild bradycardia lasting 1.5 minutes followed by an asystolic episode. B, The expanded ECG of the part inside the circle in A shows a 10-s asystolic pause due to sinus arrest followed by secondary pauses. In this case, as in all others, the exact timing of the onset of syncope cannot be defined.

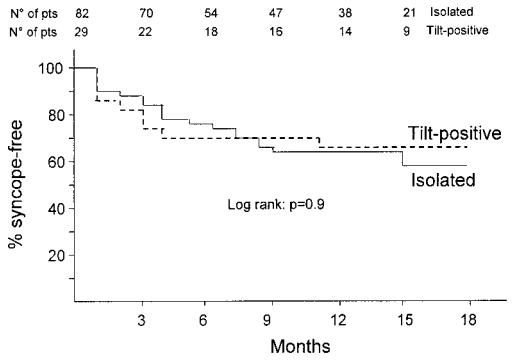

Figure 2. Kaplan-Meier estimates of the probability of remaining free of syncopal recurrences in the isolated syncope group and in the tilt-positive group.

Statistical Methods

Comparison between groups was performed with Student's *t* test or the nonparametric "U" test of Mann-Whitney, as appropriate, for continuous variables and with Fisher's exact test for proportions. The time to the onset of the events was analyzed by means of Kaplan-Meier survival curves, which were compared using the log-rank test.

Results

From November 1997 to July 2000, 111 patients (82 with isolated syncope and 29 with a positive response to tilt-testing) from 35 centers in Italy and Spain were included in the study. Patients were seen at the outpatient clinic every 3 months until the primary end point was reached, the battery of the ILR ran down, or the study ended. Follow-up was completed in October 2000. The clinical characteristics of the isolated syncope group and tilt-positive group were similar (Table 1). Although a minority of patients had some associated cardiac abnormality or disease, none had heart failure, depressed cardiac function, or heart-related impairment of their quality of life.

Isolated Syncope Group

An ILR-documented syncopal event occurred in 24 patients (29%) after a median of 105 days (range, 47 to 226 days) (Table 2). The most frequent finding, which was observed in 11 of these 24 patients (46%), was one or more prolonged asystolic pauses >3 s, mainly due to sinus arrest, which lasted for a median of 31 s (range, 20 to 44 s). In 10 of these pauses, the asystole was due to sinus arrest; in 8 it was preceded, for a few minutes, by progressive sinus bradycardia (Figure 1) and in 2, it was preceded by initial sinus tachycardia followed by progressive sinus bradycardia; one exception was that of a patient with sudden-onset atrioventricular block. Because 2 other patients had severe bradycardia <40 bpm, overall bradycardic episodes were observed in 54% of cases. The remaining patients had normal sinus rhythm or sinus tachycardia. In only 1 patient was syncope related to an ectopic atrial tachycardia.

Another 4 patients had syncope but were unable to activate the ILR. Thus, a total of 28 patients (34%) experienced a total of 37 syncopal recurrences (0.27 episodes per month). Their actuarial estimates were 15%, 34%, and 41% at 3, 9, and 15 months, respectively (Figure 2).

Presyncope occurred in 19 patients (23%); 3 of these later had a syncopal episode. Unlike syncopal episodes, presyncopal episodes were never characterized by asystolic pauses; normal sinus rhythm was the most frequent finding.

Multiple syncopal and presyncopal episodes occurred in 8 patients. Four patients with syncope and normal sinus rhythm or sinus tachycardia had a second episode of syncope with normal sinus rhythm or sinus tachycardia; 1 patient with asystolic syncope also had one episode of presyncope with bradycardia of 30 bpm; 1 patient with syncope and paroxysmal atrial tachycardia also had 2 episodes of presyncope and atrial tachycardia; finally, 2 patients had multiple episodes of presyncope with normal sinus rhythm or sinus tachycardia.

Tilt-Positive Group

The results of the tilt-positive group were very similar to those of the isolated syncope group (Table 2). An ILR-

TABLE 2. Results: Primary End Point

	Isolated (n=82)	Tilt-Positive (n=29)
Mean follow-up duration	9±5	10±5
Documented syncope, n (%)	24 (29)	8 (28)
Median time to first syncope, d (range)	105 (47–226)	59 (22–98)
Findings at the time of syncope		
Asystolic pause(s)	11 (46)	5 (62)
Maximum pause duration, s (range)	15±6 (6–24)	17±9 (3–21)
Asystole type: sinus arrest/AV block, n	9/2	5/0
Bradycardia <40 bpm, n (%)	2 (8)	1 (12)
Normal sinus rhythm, n (%)	9 (37)*	2 (25)
Sinus tachycardia, n (%)	1 (4)	0
Atrial tachycardia, n (%)	1 (4)	0

Values are mean±SD, median (range), or number of patients (%). AV indicates atrioventricular.

*Ischemia followed by ventricular fibrillation in 1 case.

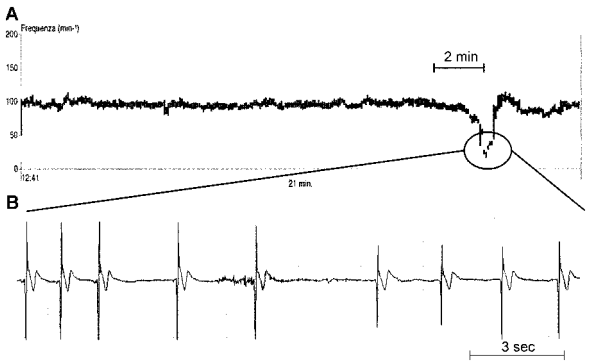

Figure 3. Tilt-positive patient. During the test, the patient had a cardioinhibitory response with an asystole of 8 s. A, Heart rate trend during 21 minutes of loop recording. Initially, the heart rate is stable at ≈100 bpm; before syncope, there is a progressively severe bradycardia lasting 2 minutes. B, The expanded ECG of the part inside the circle in A at the time of syncope shows a progressive sinus bradycardia with a maximum sinus pause of 4 s. Note the similarity with the case of isolated syncope shown in Figure 1.

documented syncopal event occurred in 8 patients (28%) after a median of 59 days (range, 22 to 98). The most frequent finding, which was observed in 5 of the 8 patients (62%), was one or more prolonged asystolic pauses, mainly due to sinus arrest, which lasted for a median of 33 s (range, 23 to 41 s); the onset of the asystolic episodes was always preceded, for a few minutes, by progressive bradycardia (3 cases) or by initial tachycardia followed by progressive bradycardia (2 cases; Figures 3 and 4). Overall, bradycardic episodes were observed in 6 cases (75%). The remaining patients had normal sinus rhythm or sinus tachycardia. No patient had syncope related to a tachyarrhythmic episode.

A correlation between the type of responses observed during tilt-testing and the spontaneous documented events was made in 8 patients (Figure 5). In general, asystolic and bradycardic events were more frequent during spontaneous recordings than during tilt-testing.

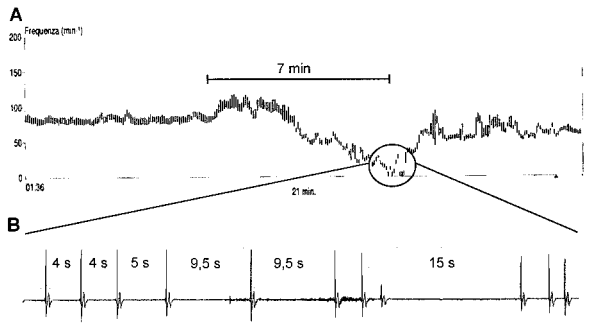

Figure 4. Tilt-positive patient. During the test, the patient had a mixed response. A, Heart rate trend during 21 minutes of loop recording. Initially, the heart rate is stable at ≈80 bpm; at the beginning of the episode, heart rate increases to 120 bpm and then progressively decreases to a very low rate. B, The expanded ECG of the part inside the circle in A at the time of syncope shows prolonged multiple pauses due to sinus arrest. Note the similarity with the case of isolated syncope shown in Figure 1.

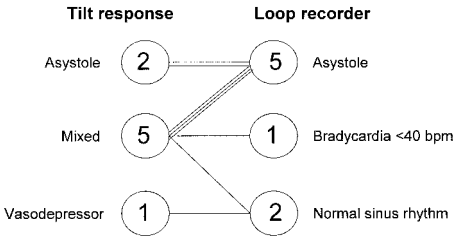

Figure 5. Correlation between tilt-induced responses and spontaneous documented syncope. Passive tilt caused one asystolic and one mixed response; nitroglycerin challenge caused one asystolic and 4 mixed responses; and isoproterenol challenge caused the vasodepressor response.

Another 2 patients had syncope but were unable to activate the ILR. Thus, a total of 10 patients (34%) had a total of 20 syncopal recurrences (0.51 episodes per month). Their actuarial estimates were 25%, 30%, and 34% at 3, 9, and 15 months (Figure 2).

Presyncope occurred in 7 patients (24%); 1 of these later had a syncopal episode. Unlike syncopal episodes, presyncopal episodes were never characterized by asystolic pauses; normal sinus rhythm was the most frequent finding (Table 3).

Multiple syncopal and presyncopal episodes occurred in 7 patients. Two patients with asystolic syncope also had a second episode of syncope with asystole; 1 patient with syncope and normal sinus rhythm had a second episode of syncope and normal sinus rhythm; 1 patient with asystolic syncope had 3 presyncopal episodes with atrial fibrillation; 2 patients had multiple episodes of presyncope with paroxysmal atrial tachycardia; and 1 patient had multiple episodes of presyncope with normal sinus rhythm.

Comparison Between Isolated Syncope and Tilt-Positive Groups

We were unable to show any statistically significant difference between groups in either the baseline characteristics or follow-up results.

Clinical Events

Only one patient (1%) experienced severe injury due to syncopal relapse; he belonged to the isolated syncope group

TABLE 3. Results: Secondary End Point

	Isolated (n=82)	Tilt-Positive (n=29)
Syncope		
Total patients with syncope	28 (34)	10 (34)
Total number of syncopal episodes	37	20
Documented syncopal episodes	32	12
Presyncope		
Total patients with presyncope	19 (23)	7 (24)
Total number of presyncope episodes	24	14
Documented presyncope episodes	20	13
Relative bradycardia	4 (20)	2 (15)
Normal sinus rhythm	8 (40)	6 (46)
Paroxysmal supraventricular tachycardia	4 (20)	5 (38)
Sinus tachycardia	4 (20)	0 (0)

Values are n (%).

and had a normal sinus rhythm at the time of the syncopal relapse. In another patient of the isolated syncope group, the ILR revealed, at the time of syncope, normal sinus rhythm with ST-T abnormalities; this was followed, some minutes later, by ventricular fibrillation, which was successfully resuscitated; the final diagnosis was vasospastic angina. One patient (isolated syncope group) experienced a stroke unrelated to syncopal events. No patient died during the study period.

At the end of the study, a permanent pacemaker was implanted in 10 patients in the isolated syncope group and in 4 patients in the tilt-positive group on the basis of the ILR findings. One patient received an implantable defibrillator and another underwent catheter ablation of atrial tachycardia.

Discussion

This study had several important results.

The patients with isolated unexplained syncope and those with a positive response to tilt-testing had similar clinical characteristics and outcome (a low recurrence rate for at least 1 year and a low risk of injury and adverse events), which suggests that they may be part of the same population.[2] The finding of a spontaneous decline in the rate of syncopal recurrence after baseline investigation has already been observed, although its mechanism remains partially unclear.[1–5] A similar recurrence rate, between 30% and 40% after 1 year, has frequently been observed in patients with a history of recurrent syncope.[2–6]

In the patients of both groups who had a documented recurrence, the most frequent finding was bradycardia at the time of the episode; typically, these patients had progressive sinus bradycardia that was most often followed by ventricular asystole due to sinus arrest or progressive tachycardia followed by progressive bradycardia and ventricular asystole due to sinus arrest; very long asystolic pauses were recorded at the time of syncope in most cases. These findings strongly suggest that, in both groups, the syncope was probably neurally-mediated and that the most frequent mechanism is a dominant cardioinhibitory reflex with prolonged asystolic pauses. The finding that syncope is mostly associated with long asystolic pauses has never been stressed before and could perhaps be regarded as typical of those forms of neurally-mediated syncope characterized by advanced age and aspecific clinical presentation without warning.

In the tilt-positive patients, asystolic syncope was also recorded despite a vasodepressor or mixed response to tilt-testing; thus, it seems that spontaneous syncope is much more frequently asystolic than one would expect on the basis of the results of tilt-testing, which cannot be used to predict the type of response of the spontaneous attack. This lack of correlation cannot be attributed to the use of isoproterenol drug challenge, which is known to cause only seldom asystolic responses, because all the patients with documented spontaneous asystolic syncopal episodes had had a positive tilting response during passive or nitroglycerin challenge (Figure 5). This finding confirms that of a small retrospective study[7] and offers an explanation regarding why pacemaker therapy is more efficacious in preventing syncopal recurrences than expected.[4]

In both groups, apart from the pattern described above, a normal sinus rhythm or sinus tachycardia was frequently recorded at the time of the syncope. This finding does not allow us to rule out definitely the possibility of a pure vasodepressor response as the cause of syncope. A reflex vasodepressor mechanism cannot be ruled out, even in the patient with syncope due to ectopic atrial tachycardia, as previously shown.[8] However, although not diagnostic, the finding of a normal sinus rhythm or tachycardia allows us to exclude an arrhythmia as the cause of syncope. Among the baseline clinical characteristics, the only feature that characterized this subset of patients was a younger age (50 ± 18 versus 65 ± 16 years; $P=0.002$).

Previously undocumented paroxysmal supraventricular tachyarrhythmia was a very infrequent cause of syncope.

Presyncope was not an accurate surrogate for syncope in establishing a diagnosis.

An excellent reproducibility of responses was observed when multiple syncopal or presyncopal episodes were documented in the same patient. This finding has a potential impact on therapy.

Comparison With Previous Studies

In the first large multicenter experience, the ILR was used in 85 patients affected by unexplained syncope.[1] The population was more heterogeneous than ours: 62% of the patients had some cardiovascular disease; no information was given about the presence of intraventricular conduction defects or other abnormalities that may suggest the cause of syncope; with the exception of Holter monitoring, diagnostic tests were not performed systematically; and, in particular, tilt-testing was performed in only 49% of patients. 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, 3 had supraventricular tachycardia, 18 had some type of "bradyarrhythmia," which was considered to be of neurally-mediated origin in 7 cases. However, when the results of that study were broken down into syncope and presyncope, bradycardia was the most frequent finding observed during syncopal episodes (in 14 of 23 patients; 69%), whereas normal sinus rhythm was frequently observed during presyncopal episodes. The number of patients with asystolic pauses was not reported.

Two single-center studies yielded contrasting results. In the initial pilot study by Khran et al,[9] syncope recurred in 15 of 16 patients with unexplained syncope, negative tilt-testing, and a negative electrophysiological study, and it was arrhythmic in 60% of cases. In a recent study by Nierop et al,[10] syncope recurred in 14 of 35 patients (40%), with normal sinus rhythm in 6, bradycardia in 4, and tachycardia in 4; in this latter study, the patients did not undergo routine tilt-testing or electrophysiological study.

In conclusion, the results of ILR studies seem to be influenced by the initial selection of the patients. Multicenter studies probably better reflect the average characteristics of the patients with recurrent syncope.

Low Sensitivity of Tilt-Testing

If isolated (tilt-negative) syncope and tilt-positive syncope have similar clinical presentation, outcome, and cause, a logical inference is that tilt-testing lacks sensitivity. The current positivity rate of tilt-testing is ≈50% to 60%,[11,12] and ≈10% of patients who have a first negative tilt-test become positive when the test is repeated.[13,14]

Presyncope Is Not Syncope

The electrocardiographic findings recorded during presyncopal episodes were different from those observed during syncopal episodes (Table 3). Although asystolic pauses due to sinus arrest were the most common finding during syncope, they were never recorded during presyncope. Normal sinus rhythm or paroxysmal tachyarrhythmias were the most common findings during presyncopal episodes. These results are similar to those of 2 other studies,[1,10] in which normal sinus rhythm was observed in 63% and 70% of presyncopal episodes. These observations suggest that presyncope cannot be considered an aborted syncope or a less severe form of syncope. Presyncopal episodes probably represent an unspecific symptom that may be due to many different mechanisms and should be interpreted with caution when considered in the context of therapeutic trials. A diagnosis should be considered established only when syncopal episodes can be detected; in such a case, that test can be regarded as the "gold standard." The recording of presyncope or asymptomatic arrhythmia, which is feasible in the new automatic version of the ILR device, leaves the diagnosis uncertain.

Limitations

Although the documentation of bradyarrhythmia concurrent with a syncopal episode is considered diagnostic, further evaluations may nevertheless be necessary to discriminate between an intrinsic cardiogenic abnormality and a neurogenic mechanism. Moreover, in the case of a patient with neurally-mediated syncope, the recording of bradycardia cannot exclude the possibility that an associated vasodepressor reflex may play an important role in the genesis of syncope and that the onset of the loss of consciousness may precede the cardioinhibitory reflex.

Although the series is relatively large for its type, the numbers are still small, and failure to detect a significant difference in the 2 groups may well be type II error.

Clinical Implications

The benign nature of isolated and tilt-positive syncope, the low recurrence rate, and the low risk of related injury we observed in the "real world" suggest a strategy of postponing treatment, in particular pacemaker therapy, until a definite diagnosis can be made by documenting a spontaneous syncopal relapse. Because presyncope did not prove to be an accurate surrogate for syncope in establishing a diagnosis, therapy should not be guided by presyncopal findings. In accordance with this approach, 16 patients (14%) underwent ILR-guided specific therapy immediately after their first syncopal documentation. Many other patients would probably have had a documented syncopal recurrence if the monitoring phase had been prolonged. The usefulness of a very prolonged monitoring phase and the efficacy of therapy in preventing further syncopal recurrences remain to be proved in prospective therapy trials. The present study forms the background for establishing such studies.

Appendix

International Study on Syncope of Uncertain Etiology (ISSUE)

Participating Centers and Investigators (number of patients in brackets)

Ospedale S. Maria Nuova, Reggio Emilia: C. Menozzi, N. Bottoni (21); Ospedale Villa Maria, Piombino: S. Tognarini, S. Bechi (8); Hospital Clinico, Barcelona: L. Mont (7); Ospedali Riuniti, Lavagna: M. Brignole, P. Donateo, G. Gaggioli (6); Ospedale Umberto I, Mestre: A. Raviele, F. Giada (6); Ospedale S. Anna, Como: G. Botto, A. Sagone(6); Ospedale per gli Infermi, Faenza: D. Cornacchia (5); Clinica S. Anna, Brescia: G. Benedini, A. Gardini (4); Ospedale Maggiore della Carità, Novara: E. Occhetta, M. Bortnik (4); Ospedale Bolognini, Seriate: P. Giani, V. Giudici, G. Leoni (4); Ospedale Fatebenefratelli e Ospedale San Filippo Neri, Roma: A. Puglisi, P. Azzolini, M. Santini, F. Ammirati (3); Hospital de Basurto, Bilbao: J.M. Ormaetxe (3); Hospital Juan Ramon Jimenez, Huelva: R. Barba, P. Morina (3); Hospital Virgen de las Nives, Granada: L. Tercedor, M. Alvarez (3); Hospital Virgen del Rocio, Sevilla: F. Errazquin (3); Hospital Clinico Universitario, Valencia: R. Garcia-Civera (2); Ospedale S. Maria Nuova, Firenze: A. Lagi (2); Ospedale Civile, Piacenza: A. Capucci, G. Villani, F. Groppi (2); Hospital Universitario, La Paz: J.L. Merino, R. Peinado (2); Ospedale Civile, Cento: P. Alboni, M. Dinelli (2); Ospedale F. Ferrari, Casarano: D. Melissano (1); Hospital Complejo Hospitalario, Leon: M. Fidalgo (1); Hospital del Mar, Barcelona: J. Martì (1); Hospital Municipal, Badalona: F. Planas (1); Hospital H. Juan Canalejo, La Coruna: L. Perez Alvarez (1); Ospedale Civile, Lugo di Ravenna: E. Tampieri (1); Ospedale Policlinico, II Università degli Studi, Napoli: L. Santangelo (1); Ospedale Lotti, Pontedera: L. Paperini (1); Ospedale della Misericordia, Udine: A. Proclemer (1); Ospedale Grande degli Infermi, Belcolle Viterbo: R. Guerra (1); Hospital Xeral de Vigo, Vigo: X. Beiras (1); Ospedale Civile, Bentivoglio: B. Sassone (1); Ospedale Civile di Oglio Po, Casalmaggiore: A. Perrini, G. Pellinghelli (1); Hospital 12 de Octubre, Madrid: F. Arrivas, M. Lopez-Gil (1); Hospital General Val d'Hebron, Barcelona: A. Moya (1).

Steering Committee

M. Brignole, R. Garcia-Civera, C. Menozzi, A. Moya

Event Committee

M. Brignole, C. Menozzi, A. Moya

Study Managers

S. Cavaglià, R. Migliorini, X. Navarro, L. Rapallini

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