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Frequent and Prolonged Asymptomatic Episodes of Paroxysmal Atrial Fibrillation Revealed by Automatic Long-Term Event Recorders in Patients with a Negative 24-Hour Holter

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ROCHE, F., ET AL.: Frequent and Prolonged Asymptomatic Episodes of Paroxysmal Atrial Fibrillation Revealed by Automatic Long-Term Event Recorders in Patients with a Negative 24-Hour Holter. *The presence, frequency, and duration of episodes of paroxysmal atrial fibrillation (PAF) is difficult to establish. This is caused by the limited duration of standard Holter recordings and to the unsatisfactory yield of patient-triggered event recorders, because of asymptomatic events and of an inconsistent use of the patient dependent triggering function. A prospective cohort of 65 consecutive patients with recurrent palpitations and a negative 24-hour ECG Holter was investigated by means of a cardiac event recorder bearing continuous automatic arrhythmia analysis and storage. Over a mean duration of 77 ± 36 hours, episodes of PAF were diagnosed in 20 (31%) patients, who had a total of 37 episodes; mean duration of PAF episodes was 7 hours 50 minutes ± 8/hours 45 minutes (minimum 45 minutes, maximum 28 hours). Eleven (55%) of these 20 patients were asymptomatic and would have remained undiagnosed without the automatic mode of the event recorder. Asymptomatic PAF episodes were longer than symptomatic ones (10 hours 30 minutes ± 6 hours 30 minutes vs 4 hours 50 minutes ± 4 hours, $P < 0.05$). In addition, episodes of sustained paroxysmal supraventricular tachycardia (PSVT) were diagnosed in 39 (57%) patients, of whom 34 (87%) were symptomatic. In this prospective cohort, a second standard 24-hour monitoring would have missed 44% of the patients with PAF or PSVT and a classical patient-triggered event recorder 13%. In patients still complaining of palpitations after one negative 24-hour Holter, numerous, prolonged, and often asymptomatic episodes of PAF can be revealed by long-term automatic event recorders. These devices should help clarify the clinical consequences of such episodes. (PACE 2002; 25:1587–1593)*

paroxysmal atrial fibrillation, arrhythmia detection, automatic cardiac event recorder

Introduction

Among cardiac arrhythmias, chronic atrial fibrillation is of particular concern because of its recognized increased risk for cerebral emboli.[1–5] However, the responsibility of the type and duration paroxysmal atrial fibrillation (PAF) in ischemic stroke has been questioned. Answers to this major issue are limited by the lack of figures about the true frequency and duration of PAF episodes and, consequently, by the difficulty to establish a clear correlation between their characteristics and cerebrovascular damages.

Repeated 24-hour Holter recordings have already demonstrated a higher prevalence of PAF episodes than previously assumed; however, available data do not result from continuous prolonged recordings, but have been extrapolated from repeated recorded samples.[6,7] Increasing recording duration has appeared as the only way to get a better knowledge of the phenomenon of PAF. The introduction of patient-triggered event recorders could have provided a proper way to this answer, since it became possible to extend monitoring duration up to 1 month, resulting in an arrhythmia detection far superior to that obtained

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using standard 24- or 48-hour recordings.[8–11] However, patient-triggered event recorders are limited in two aspects. First, PAF episodes are frequently asymptomatic and, thus, remain undetected, because patients do not use the patient-triggering function. Second, it has been found that two thirds of the patients, especially the most at risk, the elderly, are inconsistent in their use of patient-triggered devices, even when symptomatic.[12]

The aim of this study was to establish the frequency of PAF episodes in a selected population of patients suffering from recurrent palpitations but without any significant arrhythmias on a previous 24-hour Holter monitoring. For that purpose, a new device was used that combines continuous automatic electrocardiographic (ECG) event analysis and storage with prolonged monitoring duration.[13]

Patients and Methods

Patient Population

The study investigated a cohort of 65 (45 men, 20 women; mean age 63 ± 8 years) consecutive patients complaining of recurrent transient episodes of palpitations that had remained undiagnosed after a standard 24-hour ECG Holter monitoring.

These patients were extracted from a population of 140 patients complaining of palpitations and referred by their cardiologist during a 6-month period to the authors' Holter reference center, which represents about 10% of the patients referred by out hospital practitioners for arrhythmias evaluation during that period. Of the 140 patients, 36 had a diagnosis established by standard Holter recording: sick sinus syndrome (n = 1), atrial tachycardia (n = 6), PAF (n = 9), and isolated premature supraventricular or ventricular beats (n = 20). Of the 104 remaining patients, only 65 long-term recordings were accepted by the cardiologists or by the patients.

Among these 65 patients, symptoms were prolonged in 20 of them and were poorly tolerated in 5. Twenty-six patients were suffering from chronic cardiovascular diseases: hypertension (n = 18), stable coronary artery disease (n = 7), and mitral valve regurgitation (n = 1). Eight had non-cardiovascular disease: hyperthyroidism (n = 2), diabetes mellitus (n = 4), and chronic obstructive pulmonary disease (n = 2).

Standard Initial 24-Hour Holter Monitoring

Standard three-lead Holter digital recorders were used to acquire the initial ECG data (Novacor, Rueil-Malmaison, France). The mean duration of the recordings was 23.1 ± 1.2 hours (range 21–24 hours). All recordings were scanned through a DuoHolter (Novacor, Rueil-Malmaison, France) and analyzed using the interactive method.

Continuous Automatic Long-Term Cardiac Event Monitoring

Such analyses were performed by an event recorder, R-Test Evolution (RTE) (Novacor, Rueil-Malmaison, France), placed on the patients using two electrodes: the first electrode was placed on the sternum and a cable linking the device to the second electrode was placed at the apex position of the heart, which resulted in a lead close to a CM5 configuration. The RTE event recorder performs a continuous ECG analysis combined with an automatic storage of abnormal events detected in a 20-minute solid-state memory with an autonomy of up to 7 days. In addition, the patient is given the possibility to trigger a recording for a user-programmed amount of memory. Both types of recordings, automatic and patient-triggered, are based on a loop memory. The RTE is programmed to recognize ten categories of arrhythmic events and one category of ischemic events. The algorithm of arrhythmia analysis is based first on detection of a QRS prematurity or delay then, and only when this first condition is fulfilled, on QRS width. Without the prematurity or delay trigger, the RTE does not perform an arrhythmia analysis. There are six categories of premature events, the degree of prematurity of which is user-defined: (1) narrow single premature beats, (2) wide single premature beats, (3) 2–5 consecutive narrow premature beats, (4) 2–5 consecutive wide premature beats, (5) 6 or more consecutive narrow premature beats, and (6) 6 or more consecutive wide premature beats. Other arrhythmic events are absolute pauses, the duration of which is user-defined; relative pauses, of which the percentage of shortening is user-defined; and bradycardia, the rate of which is also user-defined. The last category of recorded events is ST-segment abnormality; the threshold values for the depth and the slope of the ST-segment depression are user-defined. In addition, a heart rate trend covering the whole recording period is systematically memorized.

The patients were instructed to report any clinical abnormality which would have occured during the recording. They were taught to note the description and the true occurrence of any clinical symptom.

Events Considered in the Analysis

Only sustained (≥ 30 s) paroxysmal supraventricular tachycardic events (PAF and PSVT) were considered for this analysis. PSVT

was defined as a tachycardia characterized by a heart rate ≥ 120 beats/min and lasting at least 30 seconds, with normal QRS morphology. PAF was defined as fine oscillations in the baseline ECG (fibrillatory waves) associated with an irregular ventricular response ratio and lasting at least 30 seconds. The 30-second limit of sustained paroxysmal events was based on the fact that this duration is generally admitted at the ventricular level as a criteria for sustained events. For an event of any length, sinus rhythm was considered restored after five consecutive sinus beats had been observed. Both events, PAF and PSVT, were classified as symptomatic or asymptomatic; events were considered as symptomatic if there was a temporal correspondence between the symptoms described in the patient logbook and the occurrence of PAF or PSVT in the recording.

Also, the RR trend recorded over the full monitoring period is of help in separating sustained PSVT from PAF. PSVT presents with a sudden rise in heart rate but the trend line remains thin. Conversely, the sudden acceleration of PAF episodes is associated to a important thickening of the trend line, due to the large variations in RR interval lengths that remain plotted on the trend.

Statistical Analysis

Statistical analysis were performed using Statview 4.5 from SAS (Cary, NC, USA). Comparisons between continuous variables were made using a Student's *t*-test for unpaired data. Comparisons between discrete variables were made using a chi-square test. The respective yields of the patient-triggered and the automatic modes of the RTE were compared using Kaplan-Meier cumulated survival analysis.

Results

Standard 24-Hour Holter Monitoring

All patients were free of PAF or sustained PSVT episodes on the initial 24-hour Holter recording, which was one of the inclusion criteria.

The number of isolated supraventricular beats on the initial 24-hour recordings was unrelated with the absence or presence of sustained supraventricular tachycardic events identified later using RTE (mean ± SD number of isolated supraventricular beats: 24 ± 30/hour vs 28 ± 87/hour, respectively; P = NS).

Continuous Automatic Event Recorder

Arrhythmias will be described in terms of episodes of arrhythmias and of patients with arrhythmias. The mean ± SD recording duration was 77 ± 36 hours (range 24–144 hours). Among the 65 patients, 52 (80%) had sustained supraventricular arrhythmias: 20 (31%) presented with PAF episodes, 39 (60%) PSVT episodes, and 7 (9%) patients had both arrhythmias.

PAF

A total of 37 episodes of PAF were detected in 20 patients; these episodes were distributed as follows: 1 single episode in 10 patients; two episodes in 5 patients; 3 episodes in 4 patients; and 4 episodes in 1 patient (Fig. 1). The exact duration of PAF episodes was unknown in 11 of the 37 episodes either because the episode began before the hook up of the device (n = 6), or because it ended after its removal (n = 5). The mean ± SD duration of the remaining 26 episodes was 7 hours 50 minutes ± 8 hours 45 minutes (range 45 minutes to 28 hours).

Among the 37 episodes of PAF diagnosed, only 12 (32%) of them were contemporary with symptoms. Symptomatic PAF episodes were significantly shorter than asymptomatic ones (mean ± SD, 4 hours 50 minutes ± 4 hours vs 10 hours 30 minutes ± 16 hours 30 minutes, respectively; $P < 0.05$).

The mean ± SD time interval between the hookup of the RTE and the beginning of the first PAF episode was 16 hours 30 minutes ± 21 hours (range 0–77 hours).

When considering patients, 10 (50%) of the 20 patients with PAF or PAF plus PSVT never experienced symptoms during PAF episodes; similarly 7 (54%) of the 13 patients presenting only with PAF episodes were asymptomatic.

The mean ± SD duration of PAF in the 13 PAF only patients was significantly longer than the duration of PAF episodes in the 7 patients presenting with both PAF and PSVT (10 hours 40 minutes ± 8 hours 39 minutes vs 2 hours 30 minutes ± 2 hours 14 minutes; $P < 0.01$).

PSVT

A total of 134 episodes of PSVT were observed in 39 (60%) patients. These episodes were distributed as follows: 1 episode in 3 patients, 2 episodes in 8 patients, 3 episodes in 8 patients, 4 episodes in 13 patients, 5 episodes in 4 patients, 6 episodes in 2 patients, and 7 episodes in 1 patient (Fig. 2). The exact duration of PSVT was unknown in one episode, because it began before the hookup of the event recorder. The mean ± SD duration of the remaining 133 episodes was 32 ± 136 minutes (range 3 minutes to 24 hours).

Among the 134 episodes of PSVT detected, most of them, 105 (78%), were contemporary with symptoms. The duration of symptomatic and asymptomatic PSVT episodes were not different

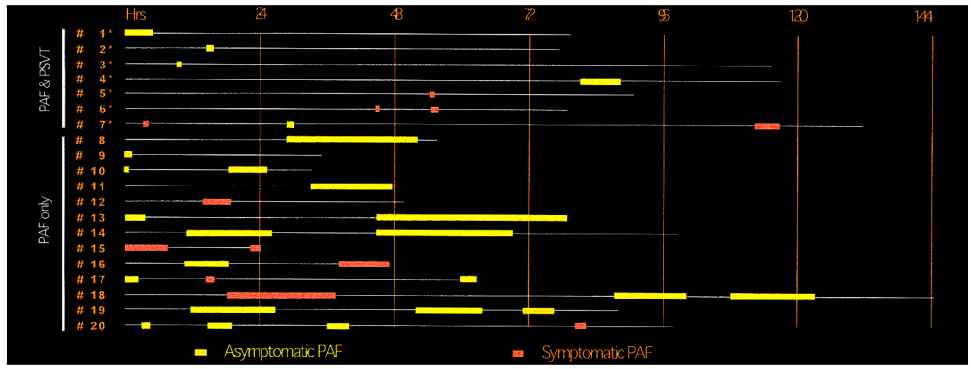

Figure 1. *Occurrence of episodes of paroxysmal atrial fibrillation (PAF) during the recording time using the R-Test Evolution. The white lines illustrate recording duration for each of the 20 patients presenting PAF episodes. The duration of the episodes of PAF are drawn in orange for symptomatic episodes and in yellow for asymptomatic ones.*

(mean ± SD: 38 ± 154 vs 14 ± 13 minutes, respectively; P = NS).

The time interval between the hookup of the RTE and the beginning of the first PSVT episode was 29 hours 32 minutes ± 21 hours 46 minutes (range 2–76 hours).

Only 5 (16%) of the 32 patients with PSVT were asymptomatic, and all 7 patients with both supraventricular arrythmias had at least one episode of symptomatic PSVT.

The duration of PSVT in PSVT only patients was not significantly different from the duration of PSVT episodes in the seven patients presenting with PSVT and PAF (36 minutes ± 2 hours 28 minutes vs 14 minutes ± 18 minutes; P = NS).

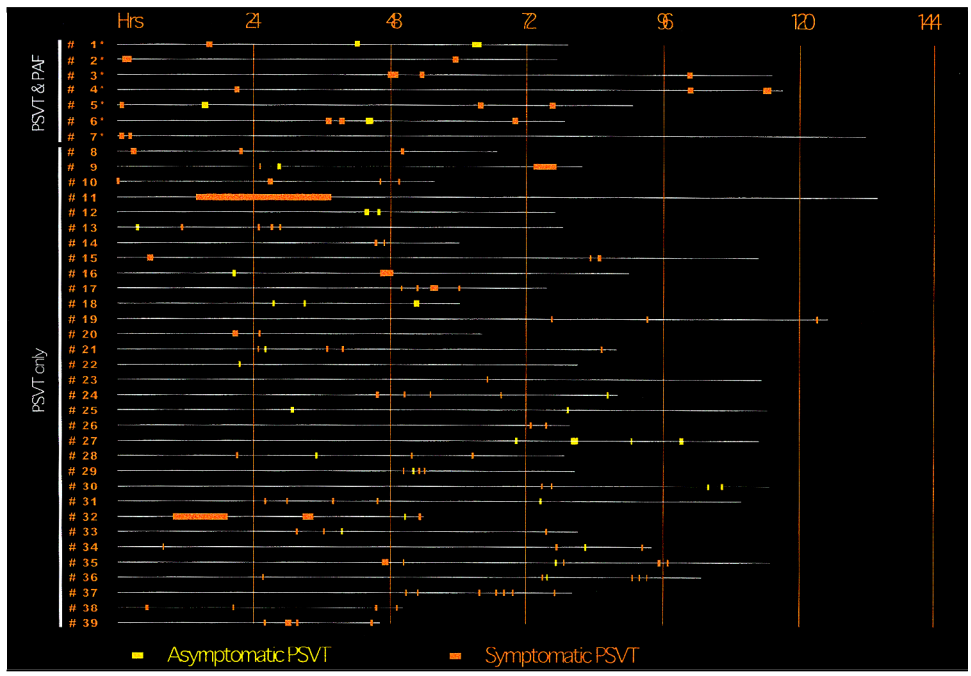

Figure 2. *Occurrence of episodes of paroxysmal supraventricular tachycardia (PSVT) during the recording time using the R-Test Evolution. The white lines illustrate recording duration for each of the 39 patients presenting PSVT episodes. The duration of the PSVT episodes are drawn in orange for symptomatic episodes and in yellow for asymptomatic ones.*

PAF and PSVT

Five of the seven patients with both types of arrhythmias described symptoms during them but, only during their PSVT episodes in two of them. The order of appearance and of recurrence of the type of arrythmia seemed to occur at random. A significant difference in symptomatology was found between the two types of arrhythmias as 11 (54%) of the 20 patients demonstrating PAF experienced no symptom during these episodes while 34 (87%) of the 39 patients with PSVT were symptomatic ($P > 0.002$).

Other Arrhythmias

Only one symptomatic nonsustained ventricular tachycardia was recorded in one patient presenting with hypertrophic cardiomyopathy.

Estimated Yield of Repeated 24-Hour Holter Recordings

On the whole, automatic continuous event recording of a mean duration of 77 hours provided a plausible explanation for palpitations in 53 (81.5%) of the 65 patients, including the one with ventricular tachycardia.

When considering only the first 24-hour period of each RTE recording, a simultaneous 24-hour Holter recording which, thus, would have been the second 24-hour standard Holter recording for the 52 patients with PAF, PSVT, or both, would still have remained negative in 23 patients because of a later onset of their arrhythmias: 2 (15%) of 13 PAF only patients, 20 (63%) of 32 PSVT only patients, and 1 (14%) of 7 patients with both types of arrhythmias. *The remaining 29 patients include the 7 patients* whose arrhythmias began before hook up of the device (six PAF and one PSVT). Thus, in 23 (44%) patients with PAF or PSVT, a diagnosis would have been missed by a second separate 24-hour Holter recording but was revealed by the RTE.

The whole recording duration of RTE monitoring in patients presenting PAF only was equivalent to 34 periods of 24-hour standard Holter recording. Among these 34 periods, 9 (27%) of them were entirely free of arrhythmic events (Fig. 1). For PSVT only patients, there were 39 (39%) out of 100 equivalent of consecutive 24-hour periods (Fig. 2) free of events, while patients presenting with both types of arrhythmias (first seven patients, Figs 1 and 2), had 10 (39%) out of 26 equivalent of 24-hour periods free of events.

Estimated Yield of Standard Patient-Triggered Event Recorders

If the number of patients who were symptomatic are extrapolated from their arrhythmias during continuous automatic event recording, 12 (23%) of the 52 patients would not have called during these periods of recording. This figure would have varied according to the type of arrhythmia, with 7 (54%) of 13 noncalling for PAF only patients, 5 (16%) of 32 noncalling for PSVT only patients, and 0 (0%) of 7 noncalling for patients having both types of arrhythmia.

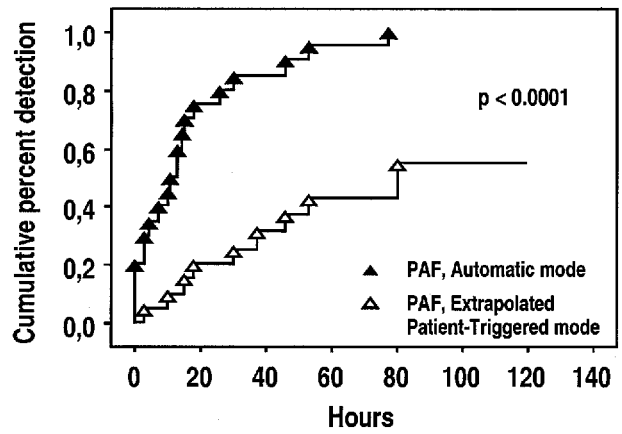

Figure 3. *Cumulative percent of patients with a episode of paroxysmal atrial fibrillation detected using the automatic mode of the R-Test Evolution (▲) or considering the yield of the extrapolated patient-triggered mode while symptoms were occurring (Δ).*

The yield of the detection of PAF episodes using the automatic mode would thus have been significantly higher than that of the patient-triggered mode ($P < 0.0001$, Fig. 3) on this relatively short recording duration. In particular, the steep increase in the cumulative percent of PAF detection obtained by means of the automatic mode would drastically contrast with the slow increase expected with the classic patient-triggered mode.

Discussion

In a population of patients still complaining of palpitations after one negative standard 24-hour Holter recording, long-term automatic continuous cardiac event monitoring revealed numerous and prolonged episodes of PAF or PSVT in 80% of them, most of which were asymptomatic. A second standard 24-hour Holter monitoring would have left 44% of the patients with such arrhythmias undiagnosed and a classic patient-triggered event recorder 13%. It is true that in four patients, PAF or PSVT were still present at the time of the removal of the device and, thus, could have been diagnosed by a standard ECG performed at that time. However, it is unclear if such a diagnosis could have been established had the event recorder not been placed.

The temporal and causal relation between atrial fibrillation and stroke is well established[2,5,14–23] and available data converge to support the prescription of preventive long-term full anticoagulation in PAF patients. However, the automatic mode of the RTE clearly confirmed the frequent lack of symptomatology in PAF. In addition, the automatic mode of the RTE clearly revealed that a lack of symptomatology was much more frequent than previously thought in PAF, which raises new questions about the relation between the frequency and the duration of PAF episodes and cerebral embolic events. In that perspective, these limited data open new frontiers in enabling such a relation to be established, provided that a significant number of patients be studied and that a long enough clinical follow-up be performed.

The benefits of a long duration of recording have already been demonstrated by a prolonged use of standard Holter, on a continuous or on a discontinuous basis. Extrapolating data from 5 weekly repeated 24-hour Holter monitoring, asymptomatic PAF episodes were described to occur more than 12 times as often as symptomatic ones.[6,7] However, such a standard Holter technique cannot be applied for time periods as long as with the RTE because of the induced discomfort for the patient. Conversely, the RTE presents as an ultracompact device and bears the convenient possibility of unweaving it, for example, during washing. This makes it a good choice for long-term automatic monitoring.

A disadvantage of the event recorder presented here lies in the lack of full recording storage. This makes incomplete the analysis and may eventually sometimes limit the strength of arrhythmia interpretation, particularly of short episodes. However, the present study clearly underlines the improved yield of long-term, automatic monitoring associating a good tolerance, a high sensitivity, and a confortable use during the active daily life.

In the present study, automaticity of the event recorders appeared as important as, or even more important than, recording duration. This parameter is of particular interest when considering that more than two thirds of the most concerned population, the elderly, are inconsistent in their use of nonautomatic event recorders, when a voluntary participation of the patient is requested to activate a record.[12] Inability to freeze tracings contemporarily with a symptomatic event has also been shown to reach 10% in implantable loop recorders.[24] The observed high percentage of asymptomatic PAF episodes should convince one towards the choice of an automatic device. However, whether automatic event recorders should replace standard 24-hour Holter to document arrhythmias in patients suffering from palpitations cannot be answered by this study, since the authors focused on a selected population with a negative standard Holter.

Knowledge of the statistical distribution of PAF episodes could allow one to optimize recording duration, which could be shorter than the presently 3 weeks proposed for patient-triggered event recorders. Nevertheless, based on the results, it is suggested that monitoring periods using automatic cardiac event recorders should not be shorter than at least 72 hours.

On the whole, automatic event recorders appear to be a powerful tool for the internist, the cardiologist, and the neurologist. The findings also suggest that epidemiological studies using such devices could allow a better description of the natural course of atrial fibrillation and of its clinical consequences, and more particularly so in the population suffering from PAF.

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References

1. Gustafsson C, Britton M. Pathogenetic mechanism of stroke in nonvalvular atrial fibrillation: Follow-up of stroke patients with and without atrial fibrillation. J Intern Med 1991; 230:11–16.
2. Wolf PA, Dawber TR, Thomas HE, et al. Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: The Framingham study. Neurology 1978; 28:973–977.
3. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation: A major contributor to stroke in the elderly. The Framingham Study. Arch Intern Med 1987; 147:1561–1564.
4. Kannel WB, Abbott RD, Savage DD, et al.: Epidemiologic features of chronic atrial fibrillation: The Framingham study. N Engl J Med 1982; 306:1018–1022.
5. Yamanouchi H, Tomonaga M, Shimada H, et al. Nonvalvular atrial fibrillation as a cause of fatal massive cerebral infarction in the elderly. Stroke 1989; 20:1653–1656.
6. Page RL, Wilkinson WE, Clair WK, et al. Asymptomatic arrhythmias in patients with symptomatic paroxysmal atrial fibrillation and paroxysmal supraventricular tachycardia. Circulation 1994; 89:224–227.
7. Clair WK, Wilkinson WE, McCarthy EA, et al. Spontaneous occurrence of symptomatic paroxysmal atrial fibrillation and paroxysmal supraventricular tachycardia in untreated patients. Circulation 1993; 87:1114–1122.
8. Kinlay S, Leitch JW, Neil A, et al. Cardiac event recorders yield more diagnoses and are most cost-effective than 48-hour Holter monitoring in patients with palpitations. A controlled clinical trial. Ann Intern Med 1996; 124:16–20.
9. Zimetbaum P, Kim KY, Ho KKL, et al. Utility of patient-activated cardiac event recorders in general clinical practice. Am J Cardiol 1997; 79:371–372.
10. Zimetbaum P, Josephson ME. Evaluation of patients with palpitations. N Engl J Med 1998; 338:1369–1373.
11. Zimetbaum PJ, Kim KY, Josephson ME, et al. Diagnostic yield and optimal duration of continuous-loop event monitoring for the di-

agnosis of palpitations. The cost-effectiveness analysis. Ann Intern Med 1998; 128:890–895.
12. Linzer M, Prichett ELC, Pontinen M, et al. Incremental diagnosis yield of loop electrocardiographic recorders in unexplained syncope. Am J Cardiol 1990; 66:214–219.
13. Roche F, Gaspoz J-M, Pichot V, et al. Accuracy of an automatic and patient-triggered long-term solid memory ambulatory cardiac event-recorder. Am J Cardiol 1997; 80:1095–1098.
14. Flegel KM, Shipley MJ, Rose G. Risk of stroke in non-rheumatic atrial fibrillation [published erratum appears in Lancet 1987; 1:878]. Lancet 1987; 1:526–529.
15. Cerebral Embolism Task Force: Cardiogenic brain embolism. The second report of the Cerebral Embolism Task Force [published erratum appears in Arch Neurol 1989; 46:1079]. (comments) Arch Neurol 1989; 46:727–743.
16. Cabin HS, Clubb KS, Hall C, et al.: Risk for systemic embolization of atrial fibrillation without mitral stenosis. Am J Cardiol 1990; 65:1112–1116.
17. Aronow WS, Ahn C, Mercando AD, et al. Correlation of paroxysmal supraventricular tachycardia, atrial fibrillation, and sinus rhythm with incidences of new thromboembolic stroke in 1476 old-old patients. Aging Clin Exp Res 1996; 8:32–34.
18. Aronow WS, Ahn C, Gutstein H. Prevalence of atrial fibrillation and association of atrial fibrillation with prior and new thromboembolic stroke in older patients. J Am Geriatr Soc 1996; 44:521–523.
19. Broderick JP, Phillips SJ, O'Fallon WM, et al. Relationship of cardiac disease to stroke occurrence, recurrence, and mortality. Stroke 1992; 23:1250–1252.
20. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: The Framingham Study. Stroke 1991; 22:983–988.
21. Jorgensen HS, Nakayama H, Raaschou HO, et al. Silent infarction in acute stroke patients. Prevalence, localization, risk factors, and clinical significance: The Copenhagen Stroke Study. (comments) Stroke 1994; 25:97–104.
22. Jerntorp P, Berglund G. Stroke registry in Malmo, Sweden. Stroke 1992; 23:357–361.
23. Harrison MJ, Marshall J. Atrial fibrillation, TIAs and completed strokes. Stroke 1984; 15:441–442.
24. Krahn AD, Klein GJ, Yee R, et al. Use of an extended monitoring strategy in patients with problematic syncope. Circulation 1999; 99:406–410.