

Noninvasive Cardiac Monitoring for Detecting Paroxysmal Atrial Fibrillation or Flutter After Acute Ischemic Stroke

A Systematic Review

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Background and Purpose—Identifying paroxysmal atrial fibrillation/flutter is an essential part of the etiological workup of patients with ischemic stroke. However, there is controversy in the literature regarding the use of noninvasive cardiac rhythm monitoring with previous reviews reporting a low detection rate with routine monitoring. We performed a systematic review to determine the frequency of occult atrial fibrillation/flutter detected by noninvasive methods of continuous cardiac monitoring after acute ischemic stroke or transient ischemic attack.

Methods—Studies were identified from comprehensive searches of PubMed, EMBASE, Science Citation Index, and bibliographies of relevant articles. Only English language articles were included. Randomized controlled trials and prospective cohort studies of consecutive patients with acute ischemic stroke that fulfilled predefined criteria were eligible. Two authors conducted searches and abstracted data from eligible studies independently.

Results—Sixty studies were deemed potentially eligible. After application of eligibility criteria, 5 studies (736 participants) were included in the analysis. All studies evaluated Holter monitoring; 2 also evaluated event loop recording. In studies that evaluated Holter monitoring (588 participants), new atrial fibrillation/flutter was detected in 4.6% (95% CI: 0% to 12.7%) of consecutive patients with ischemic stroke. Duration of monitoring ranged from 24 to 72 hours. Two studies (140 participants) evaluated event loop recorders after Holter monitoring. New atrial fibrillation/flutter was detected in 5.7% and 7.7% of consecutive patients in these 2 studies.

Conclusions—Screening consecutive patients with ischemic stroke with routine Holter monitoring will identify new atrial fibrillation/flutter in approximately one in 20 patients. Although based on limited data, extended duration of monitoring may improve the detection rate. Further research is required before definitive recommendations can be made. (*Stroke*. 2007;38;2935-2940.)

Key Words: ambulatory electrocardiography ■ atrial fibrillation ■ ischemic stroke ■ systematic review
■ transient ischemic attack

Atrial fibrillation/flutter (AF), a strong risk factor for stroke, is arguably the most important finding on cardiac workup in patients with ischemic stroke.¹⁻⁶ Once identified, introduction of oral anticoagulant therapy (eg, warfarin; international normalized ratio 2 to 3) provides an additional 40% risk reduction in recurrent stroke compared with antiplatelet therapy.⁷⁻¹⁰ Furthermore, recent evidence suggests that therapeutic oral anticoagulation (international normalized ratio 2 to 3) may also be associated with reduced stroke severity, if ischemic stroke does occur in patients with AF.^{11,12} Given that ischemic stroke with AF is associated with greater disability and mortality than those without AF, establishing the presence of underlying AF is of clear clinical importance.^{3,13-15}

In addition to baseline electrocardiogram and clinical examination, noninvasive cardiac monitoring is used to detect AF.¹⁶⁻¹⁹ A previous review on this topic reported that 24- to

48-hour Holter monitoring identified AF in 1% to 5% of patients undetected by initial electrocardiogram.²⁰ Currently, there is no clear recommendation on whether routine Holter monitoring is indicated in unselected patients with acute ischemic stroke or transient ischemic attack.²⁰ Furthermore, many of the studies included in that review were conducted at a time when the clinical significance of paroxysmal AF was underappreciated.²¹⁻²⁵ It is now acknowledged that paroxysmal AF is associated with a comparable increase in risk of ischemic stroke as continuous AF.⁶ Moreover, since the previous review of this topic, a number of studies evaluating the use of Holter monitoring, and newer methods that allow more prolonged periods of monitoring, have been published. We performed a systematic review to determine the frequency of occult AF detected by noninvasive methods of continuous cardiac rhythm monitoring in consecutive patients with ischemic stroke.

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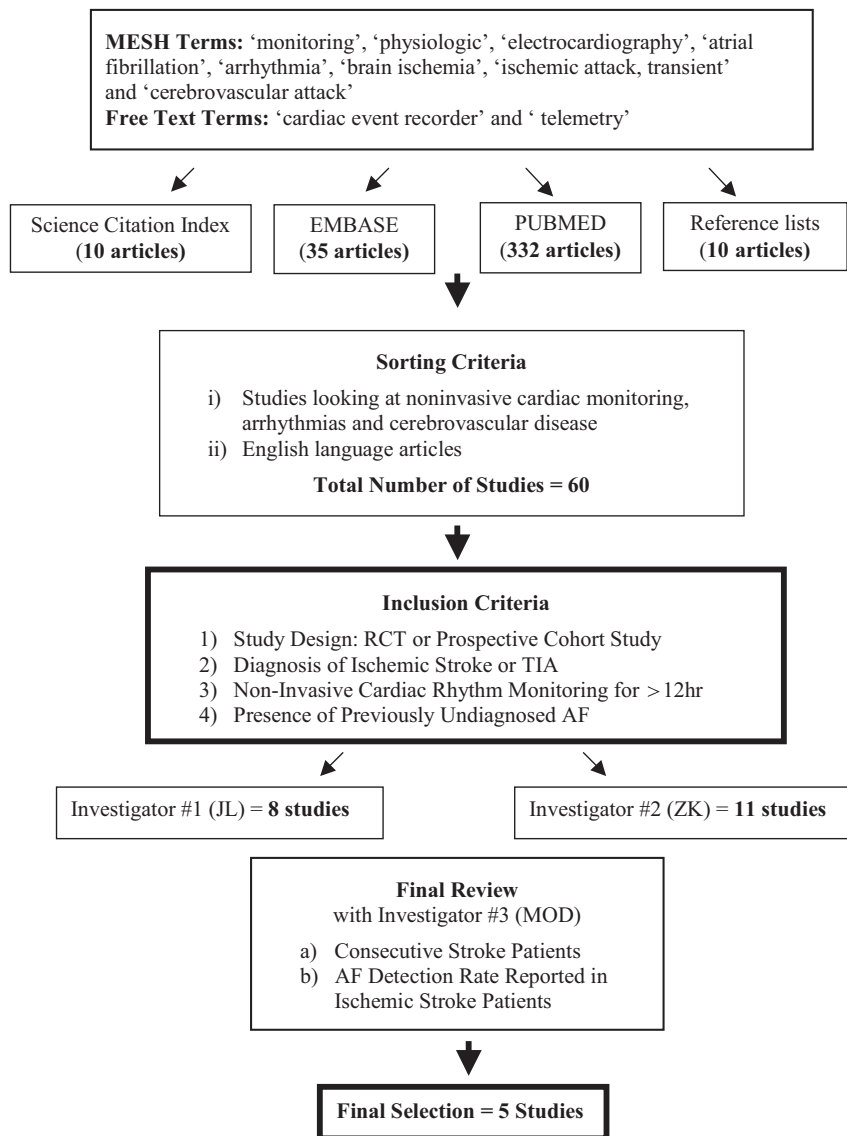


Figure. Selection process.

Methods

Data Sources

Studies were identified from the PubMed and EMBASE databases between 1966 and May 2006 by crossreferencing the following MeSH terms: "monitoring, physiological" and "electrocardiography, ambulatory" with "atrial fibrillation/diagnosis," "arrhythmia" as well as with "stroke," "brain ischemia," "ischemic attack, transient," and "cerebrovascular accident." The free text terms "cardiac event recorder" and "telemetry" were used in all searches. After finding all potentially relevant articles, reference lists were examined as well as "relevant articles" links. Science Citation Index was used to identify additional studies. Two investigators independently conducted searches. Articles were limited to those in the English language. A research librarian assisted in our search strategy.

Study Selection

Two investigators independently reviewed all studies identified on the search. For inclusion, studies were required to fulfill the following inclusion criteria: (1) study design: (a) randomized, controlled trials in which patients are randomized to receive noninvasive cardiac monitoring compared with control or (b) prospective cohort studies; (2) population: consecutive patients with a diagnosis of acute ischemic stroke or transient ischemic stroke; (3) interven-

tion: participants underwent noninvasive rhythm monitoring to detect AF for a minimum duration of 12 hours; and (4) outcome: frequency of AF detected by noninvasive monitoring was reported.

Data Abstraction

Data abstraction was conducted independently by two investigators (J.L., Z.K.) using standardized data abstraction forms developed before searches were conducted.

Statistical Analysis

The study-specific effect estimates were combined using a precision-weighted (ie, reciprocal of the variance), random-effects model and 95% CIs were calculated. Zelen's exact test was used to determine whether there was statistical heterogeneity between individual studies. A 95% CI that did not include one was considered to be statistically significant. Minitab 14.3 statistical software was used for the analyses. The following factors were hypothesized, a priori, to influence the detection rate of AF: duration and timing of monitoring, stroke subtype and severity, and setting.

Results

Study Identification and Selection

The initial search identified 387 studies, reduced to 60 potentially eligible studies that fulfilled our sorting criteria.

Table 1. Study Characteristics

Study, Year	Design	Inclusion and Exclusion Criteria	N	Intervention	Outcomes	Comments
Barthelemy et al, 2003	PCS	Inclusion: ischemic stroke or TIA; exclusion: any other neurological pathology including metabolic, epilepsy, migraine	60	Cardiac event recorder	AF	None
Hornig et al, 1996	PCS	Inclusion: ischemic stroke or TIA	300	Holter monitor	AF	87% underwent Holter monitoring
Jabaudon et al, 2004	PCS	Inclusion: acute stroke or TIA; exclusion: previous AF, recent PAF, hemorrhagic stroke, acute large vessel dissection	149	Holter monitor, event loop recorder	AF and flutter	27% refused ELR
Rem et al, 1985	PCS	Inclusion: cerebral infarction, TIA; exclusion: ICH, tumor, SAH, syncope	184	Continuous cardiac monitoring, Holter monitor	AF, arrhythmia	30% underwent Holter monitoring; 2 participants without admission ECG
Schuchert et al, 1999	PCS	Inclusion: acute ischemic stroke likely embolic in origin, NSR; exclusion: history of AF or flutter, evidence of carotid lesions or intracardiac thrombus	82	Holter monitor	AF	Narrow inclusion criteria: only participants with likely cardioembolic stroke

PCS indicates prospective cohort study; TIA, transient ischemic attack; PAF, paroxysmal atrial fibrillation; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; NSR, normal sinus rhythm; ELR, event loop recorder; ECG, electrocardiogram.

After application of eligibility criteria, 5 prospective cohort studies (736 participants) were eligible^{24,26–29} (Figure). No randomized, controlled studies were identified. Tables 1 and 2 describe the population, sample size and intervention in each of the individual studies.

Frequency of Atrial Fibrillation and Atrial Flutter Detected by Routine Cardiac Monitoring

Five studies (588 participants) evaluated Holter monitoring in the inpatient setting.^{24,26–29} In these studies, rates of detection of new AF ranged from 3.8% to 6.1% (Table 3). When the results of these studies were combined in a random-effects model, new AF was detected in 4.6% (95% CI: 0% to 12.7%) of consecutive patients with ischemic stroke independent of baseline electrocardiogram and clinical examination (test for heterogeneity $P=0.9$). Two studies (140 participants) evaluated event loop recorders after Holter monitoring.^{26,28} New AF was detected in 5.7% and 7.7% of consecutive patients in these 2 studies. One

study (159 participants) evaluated continuous cardiac monitoring using inpatient telemetry (48 hours) and detected new AF in 2.5% of participants²⁴ (Table 3).

Stroke Subtype, Stroke Severity, and Setting

Two studies reported the frequency of AF within ischemic stroke subtypes.^{26,28} In the largest of these studies ($n=149$), most cases of AF were detected in patients with total and partial anterior circulation ischemic strokes (68%), whereas no cases of AF were identified in patients with lacunar stroke.²⁸ In the other study, no significant association between AF and stroke subtype was reported.²⁶

Two studies reported stroke severity in participants with and without AF.^{27,28} Jabaudon et al²⁸ reported more severe neurological deficit (National Institutes of Health Stroke Scale ≥ 10) in patients with AF (22.7%) compared with patients without AF (3.1%). ($P=0.003$)²⁷ Hornig et al²⁵ did not report an association between stroke severity and AF. No

Table 2. Patient Characteristics

Study, Year	N	Mean Age	Female	History of Atrial Fibrillation/Flutter	History of Stroke or TIA	Risk Factors (%)				
						HTN	DM	Hyperlipidemia	Smoking	History of CAD or MI
Barthelemy et al, 2003	60	64	45%	ND	26.7%	50	6.7	50	36.7	ND
Hornig et al, 1996	300	59	38.7%	ND	45%	43.7	34	64.3	28.7	ND
Jabaudon et al, 2004	149	69	32.2%	4.7%	16.8%	58.4	16.8	55.7	34.9	16.8
Rem et al, 1985	184	63.5	33.7%	12.0%	31.5%	56.5	16.3	ND	39.1	31.5
Schuchert et al, 1999	82	*	42.7%	None	ND	36.6	ND	ND	ND	16.9

*AF group mean: 70; non-AF group: 59.

TIA indicates transient ischemic attack; HTN, hypertension; DM, diabetes mellitus; CAD, coronary artery disease; MI, myocardial infarction; ND, no data.

Table 3. Study Results

Study, Year	N	Intervention	Duration of Monitoring	Definition of Atrial Fibrillation	New Atrial Fibrillation/Flutter	Initiation of Monitoring
Barthelemy et al, 2003	60	Cardiac event recorder (n*=52)	4 days (70.1 hours)	≥30 seconds	7.7%	10 days from stroke event
		Holter monitor (n=55)	24 hours		5.5%	Admission to neurology ward
Jabaudon et al, 2004	149	Holter monitor (n=139)	21 hours	Not stated	5.0%	8 days after admission
		Event loop recorder (n=88)	159 hours	AF detected by manual review	5.7%	55 days after admission
Hornig et al, 1996	261	Holter monitor (n=261)	24 hours	Not stated; evaluated by cardiologist	3.8%	ND
Rem et al, 1985	184	Continuous cardiac monitoring (n=159)	48 hours	Not stated; evaluated by neurology resident	2.5%	ND
		Holter monitor (n=51)	24–48 hours		3.9%	ND
Schuchert et al, 1999	82	Holter monitor (n=82)	72 hours	At least 1 minute	6.1%	2–3 weeks after acute stroke

*n values indicate subjects without atrial fibrillation/flutter on history or previously.
ND indicates no data.

eligible studies included nonhospitalized patients with ischemic stroke only.^{24,26–29}

Duration and Timing of Monitoring

All studies reported the duration of monitoring.^{24,26–28} Duration of monitoring ranged from 21 to 159 hours. Studies evaluating event loop recorder monitors reported a detection rate of 5.7% after 70 hours and 7.7% after 159 hours of monitoring.

Three studies reported on the timing of initiating of monitoring from the diagnosis of stroke.^{26,28,29} One study initiated monitoring 55 days (median delay) postevent.²⁸ Two studies reported that monitoring began on admission to the ward; however, the timing from onset of stroke was unclear.^{26,28} Two studies did not report the timing of initiating of monitoring.^{24,27}

Detection of Atrial Fibrillation Resulting in a Change in Management

One study reported the proportion of patients in which the results of noninvasive monitoring resulted in a change in antithrombotic therapy.²⁸ In that study, oral anticoagulation was started in 28.6% (2 of 7) of patients with new-onset AF detected by Holter monitoring and in all 5 patients with AF detected by event loop recorder.

Discussion

Our review suggests that routine Holter monitoring in consecutive hospitalized patients with ischemic stroke detects AF in approximately one in 20 patients, beyond that detected by physical examination and initial electrocardiogram. The range of detection rates (3.8% to 6.1%) is slightly more than that reported in an earlier review by Bell et al (1% to 5%).²⁰ Our study differs from that review in a number of respects. First, we only included prospective studies. Second, most studies in the previous review were older and conducted

(>20 years ago) when the clinical importance of paroxysmal AF was not appreciated, which may have influenced whether paroxysmal AF was reported.^{21–25} Third, 2 studies included in our analysis were published subsequent to the review by Bell et al.^{26,28}

Very limited data suggest that confining Holter monitoring to patients with nonlacunar stroke may improve its diagnostic use. In the study by Jabaudon et al,²⁸ no cases of AF were reported in patients with lacunar stroke. A potential limitation of the Jabaudon study²⁸ is the unblinded evaluation of stroke subtype, which may have been biased by knowledge of the results of cardiac monitoring. One retrospective study, not included in this review, reported that Holter monitoring identified the greatest yield of AF in patients with unexplained embolic stroke.³⁰ This is further supported by the results by Schuchert et al,²⁹ which found a relatively higher detection rate of 6.1% in patients with suspected cardioembolic ischemic stroke. Furthermore, there are 2 observational studies that suggest that oral anticoagulation may not be associated with the same benefit for prevention of recurrent stroke in patients with AF presenting with lacunar stroke compared with those presenting with other ischemic stroke subtypes.^{11,31} Although based on very limited data, these observations suggest that limiting Holter monitoring to patients with nonlacunar ischemic stroke might be reasonable, but further research is required before definitive recommendations can be made.

Increased duration of monitoring appears to be associated with increased rates of detection of AF (Table 3). In the 2 studies that evaluated event loop recorders (140 participants), new AF was detected in 5.7% and 7.7% of consecutive patients in these 2 studies.^{26,29} Our review is unable to determine the optimal duration of monitoring. Similarly, the best time to initiate cardiac monitoring after a stroke is uncertain. No study explicitly evaluated and reported on early monitoring (within 48 hours) from onset of stroke symptoms.

Table 4. General Principles of Good Screening

Atrial fibrillation in acute ischemic stroke	
1. The condition should be an important problem	✓
2. The condition should be common	+/-
3. The condition should have a readily available and acceptable treatment.	✓
Holter monitoring	
4. The screening test should be accurate	✓
5. The screening procedure should have a reasonable cost	✓
6. The screening procedure should be acceptable to the patient and society.	✓

Our review has several limitations. Eligible articles were restricted to published studies in English language journals, and conference abstracts were not accessed. Thus, unpublished studies may have been overlooked. Furthermore, because only hospitalized patients were included in eligible studies, we are unable to comment on the use of Holter monitoring in the outpatient stroke population. Our strict inclusion criteria resulted in fewer numbers of eligible articles compared with a previous review. Furthermore, sample sizes of studies included were relatively small. As a result, the confidence interval about the summary estimate is wide (95% CI: 0% to 12.7%), a clear limitation of this review. However, we believe that restricting eligibility to prospective studies is an overall strength of our review.

Do the results of this review have implications for clinical practice? Should all patients with ischemic stroke be screened with Holter monitoring? If we apply the general Principles of Good Screening, we observe that Holter monitoring fulfills most criteria (Table 4).³²⁻³⁶ However, in unselected patients, it remains open to argument whether AF is insufficiently prevalent to justify routine screening.

In conclusion, screening consecutive patients with ischemic stroke with routine Holter monitoring will identify new AF in approximately one in 20 patients. Extended duration of monitoring and confining its use to patients with nonlacunar stroke may improve detection rates. However, further research is needed to evaluate extended monitoring, using newer techniques, in patients with ischemic stroke.

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Disclosures

None.

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