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High Incidence of Atrial Fibrillation or Flutter in Stroke Patients Who Have the Clinical Risk Factors for Stroke

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Abstract

The incidence of stroke in patients with atrial fibrillation or flutter (AF) is well known and depends on the presence of risk factors.The incidence of AF in patients who have a stroke and its relationship to risk factors is not as clear, however, because many stroke patients may have occult intermittent AF that is not present at the time of stroke and is not diagnosed.To better assess the incidence of AF, we studied the clinical records and all the 12 lead ECGs in a 14 year medical center data base of 985 patients admitted with ischemic stroke over a 3 year, period and correlated the incidence of AF with the presence of the stroke risk factors.Of the stroke patients with congestive heart failure 61.9% had AF (95%CL 54.4, 68.9), with age >/=75 years 45.2% had AF(CL 41.0,49.4), with coronary artery disease 42.9% had AF (CL 36.8,49.2), with diabetes 39.2% had AF (CL 32.8,46.1) and with hypertension 33.7 % had AF(CL 30.5,37.1) , all significantly higher than without these risk factors. Patients with > 1 risk factor or with echo abnormalities, especially left atrial enlargement, had an even higher incidence of AF.These findings suggest that AF may be a very common mechanism whereby the stroke risk factors cause stroke. Stroke patients in normal sinus rhythm with these risk factors should be monitored for AF so they can receive anticoagulation to prevent a subsequent stroke if AF is diagnosed.

Introduction

Many studies have confirmed that atrial fibrillation or flutter (AF) can cause ischemic stroke.[1-8] The incidence of stroke in patients with AF varies from 2 to 10.5% per year depending on the presence of risk factors.[2,4-6] The incidence of AF in patients who have ischemic strokes, however, is not as clear primarily because patients with intermittent AF have the same risk for stroke as those with persistent AF and stroke patients with intermittent AF may be in normal sinus rhythm when they present with their stroke.[6,9-12] Many patients with cryptogenic stroke have been found to have intermittent AF; the incidence of AF largely related to the length of time they were monitored post stroke.[10-15] Monitoring every stroke patient for prolonged periods is not practical. The diagnosis of AF in a patient with an ischemic stroke is important because anticoagulation of these patients can greatly decrease the high incidence (over 10%/year)[5] of a subsequent stroke.[1-4,8] To determine if the incidence of AF in stroke patients is related to the presence of the stroke risk factors, and to determine if we could identify stroke patients who would most likely have had AF on long term monitoring, we retrospectively reviewed the clinical records and all the ECGs in a 14 year data base of ischemic stroke patients admitted to a 900 bed medical center over a 3 year period.

Methods

The clinical records of all patients discharged from a 900 bed teaching/research medical center with a diagnosis of ischemic stroke (codes 434.00, 434.01, 434.11, 434.91) from January 1, 2005 to December 31, 2007 were reviewed. Patients with a mitral valve prosthesis or mitral stenosis were excluded. The diagnosis of clinical congestive heart failure (CHF), hypertension, diabetes, and coronary artery disease (CAD) (history of myocardial infarction, angioplasty, coronary artery bypass grafting) along with age and sex were tabulated. All 12 lead ECGs in the institutional data base from 1993 through December 2007 for each patient were printed out and reviewed (approximately 6000 ECGs).The presence of atrial fibrillation or flutter recorded on any ECG in the data base taken during the admission for stroke or on any emergency room visit, clinic visit or another admission before or after the admission for stroke, was determined. The available echocardiogram reports were reviewed and the presence of left atrial enlargement (LAE) (dimension >/=4.0 cm), left ventricular (LV) enlargement (LV end diastolic dimension >/=5.6 cm), and abnormal ejection fraction (<50%) were tabulated.

Disclosures:
None.

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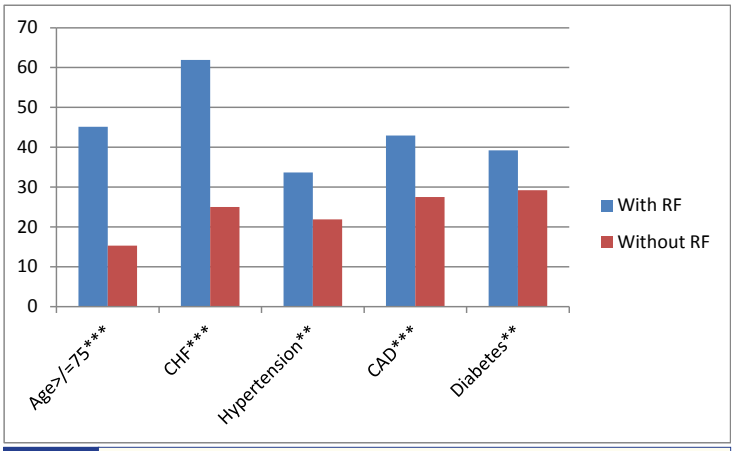

Figure 1: Total Stroke Population: Incidence of AF (%) with and without the stroke risk factors. The presence of each of the risk factors was associated with a significant increase in the incidence of AF

Abbreviations: AF-atrial fibrillation or flutter, CAD-coronary artery disease, CHF-clinical congestive heart failure, RF-risk factor. **- p<.01, ***- p<.0001

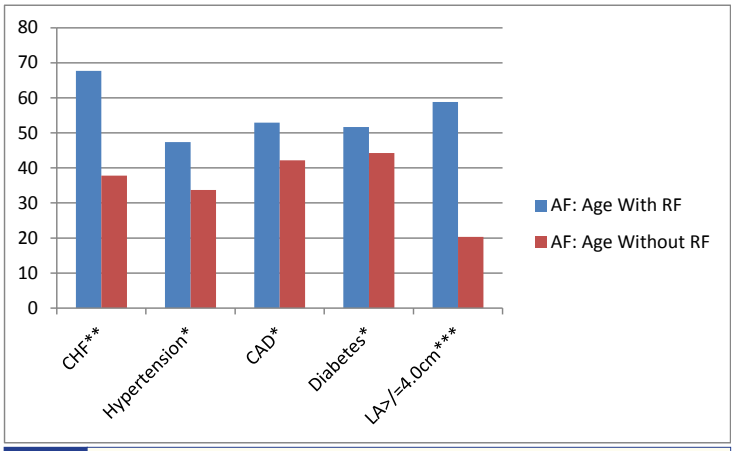

Figure 2: Stroke Patients with Advanced Age: Incidence of AF in patients >/=75 years who also have an additional risk factor. The presence of any of the other risk factors significantly increased he incidence of AF

Abbreviations: Abbreviations as on previous figures and LA-left atrium, *-P<.05

Statistics: The association between two groups of categorical variables were reviewed by 2X2 contingency tables and analyzed by Fishers exact test, with two sided p values <0.05 considered statistically significant; 95% confidence limits (CL) of individual proportions were determined (modified Wald method) (GraphPad Software Inc.)The incidence of atrial fibrillation or flutter (AF) in these ischemic stroke patients with and without one or more of the risk factors were compared and the Odds Ratio (OR) (1993-2013 MedCalc Software bvba) was determined. The stroke patients with clinical CHF were divided into those with heart failure with reduced ejection fraction (<50%), and those with preserved ejection fraction>/= 50%) and the incidence of AF was compared.

Results

Ischemic stroke was diagnosed in 985 patients. (Fig.1) CHF was present in 168 patients, 61.9% had AF (95% confidence limits (CL) 54.37, 68.91 %); Odds ratio (OR) compared to patients without CHF 4.88, p<.0001; 527 were 75 years or older, 45.2% had AF (CL 40.96,49.43%), OR 4.56 p<.0001. CAD was present in 240 patients, 42.9% had AF (CL 36.81, 49.24%), OR 1.98 p<.0001; 204 patients had diabetes, 39.2% had AF (CL 32.77, 46.06), OR 1.56, p=.0067. Hypertension was present in 784 patients, 33.7% had AF (CL 30.45, 37.06), OR 1.81, p=.0014.(Fig.1) Adding any of the other clinical risk factors to age>/=75 (Fig.2) significantly raised the incidence of AF;CHF to 67.7% AF, hypertension to 47.4% AF, CAD to 52.9% AF, diabetes to 51.7%. In stroke patients with hypertension adding CAD increased AF incidence to 43.4%, adding CHF increased AF incidence to 62.5% and adding advanced age, to 47.4% (Fig 3). Adding diabetes to hypertension did not. Adding advanced age to CHF increased the incidence of AF to 67.7% (Fig4). Adding the other clinical risk factors to CHF did not significantly increase the % of AF.

Echocardiographic diagnoses were available in 937 patients. (Fig 5) Left atrial enlargement was present in 527 patients, 47.3% had AF, significantly greater than 11.7% AF among those without

Table 1: Total Stroke Population: Incidence of AF in Patients With and Without Stroke Risk Factors

GROUP	Total Pts	Pts With AF	Percent AF
Total Pts	985	308	31.27% (95% CL 28.45, 34.23%)
Men	475	141	29.68 p=.3033
Women	510	167	32.75
>/=75	527	238	45.16 (95%CL 40.96, 49.43%, O.R. 4.56) p<.0001
<75	458	70	15.28
CHF	168	104	61.90 (95% CL 54.37, 68.91%, O.R. 4.88) p<.0001
No CHF	617	204	24.97
Hypertension	784	264	33.67 (CL 30.45, 37.06%, O.R.1.81) p=.0014
No Hypertension	201	44	21.89
CAD	240	103	42.92 (CL 36.81, 49.24%, O.R. 1.98) p<.0001
No CAD	745	205	27.52
Diabetes	204	80	39.22 (CL 32.77, 46.06%, OR 1.56) p=.0067
No Diabetes	781	228	29.19

AF-atrial fibrillation or flutter, CHF-clinical congestive heart failure, CAD-coronary artery disease, Pts-patients

Table 2: Influence of other Risk Factors on Incidence of AF in Stroke Patients >/= 75 Years Old

GROUP	AF Pts/Tot Pts	Percent AF
>/= 75 + CHF	88/130	67.69% p<.0001
>/=75 no CHF	150/397	37.78
>/=75 + Hi BP	209/441	47.39 p=.0241
>/=75 NI BP	29/86	33.72
>/=75 + CAD	79/150	52.92 p=.0329
>/=75 no CAD	159/377	42.17
>/=75 + DM	61/118	51.69 p=.0119
>/=75 no DM	181/409	44.25
>/=75 +LAE	190/323	58.82 p<.0001
>/=75 NI LA	35/172	20.35

As in table 1 and DM-diabetes, Hi BP-hypertension, LAE-left atrial enlargement, NI- normal

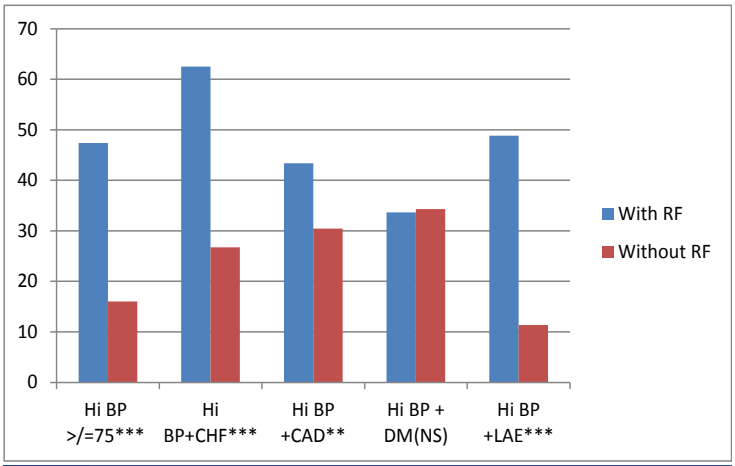

Figure 3: **Stroke Patients with Hypertension: Incidence of AF in hypertensive stroke patients with and without an additional risk factor. The presence of advance age, coronary artery disease, congestive heart failure or left atrial enlargement significantly raised the incidence of AF in these stroke patients. The presence or absence of diabetes did not affect the incidence of AF in patients with hypertension**

Abbreviations: Abbreviations as on previous figures and DM-diabetes, Hi BP-hypertension, LAE –left atrial enlargement, NS-not significant

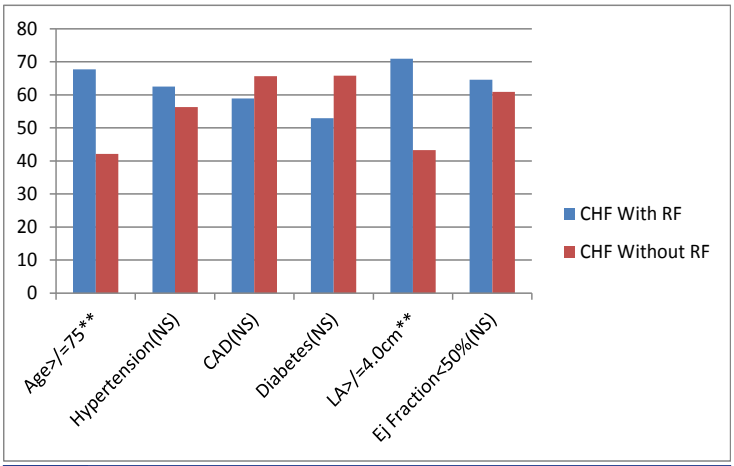

Figure 4: **Stroke Patients with CHF: Incidence of AF in patients with CHF who also have one of the other risk factors. Except for age and left atrial enlargement the presence or absence of the other risk factors in addition to clinical CHF had no significant influence on the incidence of AF. Stroke patients with clinical congestive heart failure with preserved systolic function had the same incidence of AF as did those with decreased systolic function (ejection fraction<50%)**

Abbreviations: Abbreviations as on previous figures and Ej Fraction-ejection fraction

LAE (p<.0001). The presence of LAE raised the incidence of AF to 48.8% in patients with hypertension, to 58.8% among the elderly and to 70.9% among those with CHF. In the total population of stroke patients, among those with ejection fraction (EF) less than 50%, 49.0% had AF, compared to 28.3% with EF>/= 50% (p<.0001). However among those with clinical CHF, the incidence of AF was the same regardless of the ejection fraction. The presence of LV enlargement did not affect the incidence of AF.

Of the 308 patients with AF, 190 had AF recorded on the day of admission for stroke, 108 had only sinus rhythm recorded on the admission day and 10 patients had ECGs recorded before and after the stroke admission day but no ECG recorded on the day of admission available in the data base. In the patients with sinus rhythm on the stroke admission day, 40 had an ECG showing AF prior to the stroke admission, 37 had an ECG with AF after the stroke admission and 9 had AF on ECGs recorded both before and after the stroke admission day The ECGs with AF were frequently recorded months to years before or after the stroke and some patients had numerous recordings of AF with long periods between them. In the 10 patients with no available ECG on the day of admission, 2 had AF before, 6 had AF after and 2 had AF both before and after the stroke admission; 22 patients with sinus rhythm on admission had a clinical history of AF when admitted for stroke but no ECG with AF was found in the data base. Thus 96 patients with no AF recorded on the day of admission were found to have AF using the long term hospital data base.

In these patients with AF, we found a high incidence of the stroke risk factors in both the patients who had AF on presentation to the hospital and those who were in sinus rhythm on admission but had AF found in the data base. The incidence of diabetes and coronary artery disease were similar in the 2 groups but the incidence

Table 3: **Influence of Other Risk Factors on % AF in Patients with Hypertension**

GROUP	AF Pts/Tot Pts	Percent AF
Hi BP >/=75	209/441	47.39% p<.0001
Hi BP< 75 y.o.	55/343	16.03
Hi BP+CHF	95/152	62.50 p<.0001
Hi BP No CHF	162/632	26.74
Hi BP +CAD	85/196	43.37 p=.0012
Hi BP No CAD	179/588	30.44
Hi BP + DM	72/214	33.64 p=.9328
Hi BP no DM	198/577	34.32
Hi BP +LAE	205/420	48.81 p<.0001
Hi BP no LAE	36/317	11.36

As in tables 1 and2 and y.o.-years old

Table 4: **On Incidence of AF in Stroke Patients with CHF**

GROUP	AF Pts/Tot Pts	Percent AF
CHF >/=75 y.o.	88/130	67.7% p=.0073
CHF <75 y.o.	16/38	42.1
CHF + Hi BP	93/152	62.5 p=.7878
CHF NL BP	9/16	56.3
CHF + CAD	41/72	58.9 p=.2659
CHF no CAD	63/96	65.6
CHF + DM	27/51	52.9 p=.1238
CHF no DM	77/117	65.8
CHF + LAE	90/127	70.9 p=.0033
CHF no LAE	13/30	43.3
CHF + EF<50%	42/65	64.6 p=.7383
CHF NI EF	56/92	60.9

As in previous tables and EF-ejection fraction

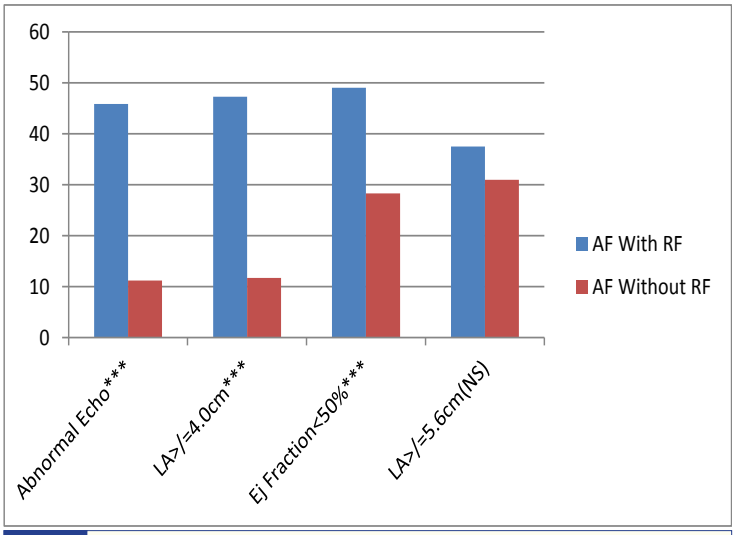

Figure 5: **Total Stroke Population: Incidence of AF (%) with and without echo abnormalities. The presence of any echo abnormality or of left atrial enlargement or decreased ejection fraction significantly increased the incidence of AF. Left ventricular enlargement alone did not significantly affect the incidence of AF**

Abbreviations: Abbreviations as on previous figures and LV- left ventricle

of CHF, hypertension, advanced age and left atrial enlargement were significantly higher in the patients with AF present on a stroke admission ECG.

Discussion

Since the report of the Framingham study in 1978,[16] nonvalvular AF has been implicated as a risk factor for strokes. Many studies[1-6] have confirmed this relationship and have demonstrated that anticoagulation will significantly decrease the incidence of ischemic stroke in patients with AF. Prospective studies in patients with AF have identified risk factors associated with AF that increase the likelihood of stroke and that are associated with an increase in the prophylactic benefit of anticoagulation.These studies have led to the development of various schema for determining which patients with non-valvular AF will benefit from anticoagulation.[2,5,6] A major problem in determining the actual importance of AF in stroke, however, has been the fact that intermittent AF carries the same risk of stroke as persistent or permanent AF.[9-12,15] This has raised the possibility that occult intermittent asymptomatic AF that is not present on admission to the hospital in many stroke patients may be playing a major role in the occurrence of stroke and that AF is under-

Table 5: **Incidence of AF in Stroke Patients With and Without Echo Abnormalities**

GROUP	Total Pts	Pts With AF	Percent AF	
Echo Abn	554	254/554	45.85%	p<.0001
NI Echo	383	43/383	11.23	
L A>/=4.0	527	249/527	47.25	p<.0001
LA<4.0	410	48/410	11.71	
EF<50%	153	75/153	49.02	p<.0001
EF>/=50%	784	222/784	28.32	
LV>/=5.6	104	39/104	37.50	p=.1813
LV<5.6	833	258/833	30.97	

As in previous tables and Abn-abnormalities, LA-left atrium, LV-left ventricle

diagnosed.[11] Identification of stroke patients in whom AF may have played a role is important because patients with AF who have had a stroke are at high risk for a recurrent stroke (greater than 10% per year),[5] and will benefit from anticoagulation.[4,8]

The purpose of this study was to correlate the incidence of AF in patients with ischemic stroke with the presence of stroke risk factors using the 14 year database of an active medical center. This data base enabled the retrieval of all of the 12 lead ECGs of patients diagnosed with an ischemic stroke recorded during any interface with the hospital, either in the ER, in a clinic or during any admission to the hospital over a long time period before and up to a few years after the stroke admission and made missing intermittent AF less likely.

We found that stroke patients with the stroke risk factors had a high incidence of AF ranging from 62% in stroke patients with CHF, 45% in patients >/= 75 years old, 43% in patients with CAD, 39% in patients with diabetes and 34% in patients with hypertension. Patients with more than one risk factor and/or with left atrial enlargement on echocardiography increased the incidence of AF, approaching or exceeding 50%.

Other methods have been utilized to demonstrate the presence of intermittent AF in patients who have had an ischemic stroke. The most common has been to prospectively monitor patients with cryptogenic stroke, i.e. no history of AF or other diagnosed cause of stroke, for varying periods of time.[11,12,14,15] The incidence of finding AF has varied directly with the length of time that monitoring occurred. The highest incidence of AF (28%) in cryptogenic stroke patients was found by Ziegler et al[15] in patients with implanted pacemakers or defibrillators that have an intrinsic monitoring capability that were followed for 1.1+/-0.7 years.Most of the other prospective monitoring studies have been disappointing with a low yield of newly diagnosed intermittent AF because there may be long intervals between episodes of intermittent AF and monitoring probably had not been continued for long enough. More selective choice of stroke patients to be monitored, i.e. those with the stroke risk factors (using the $CHADS_2$ criteria "backwards") (17,18) would probably have increased the yield. We recently reported a retrospective study of 128 stroke patients who had implanted devices using both the clinical history of AF and the presence of AF in the ECG data base (17 years).[19] We found that 71.1% of the stroke patients had findings of AF.

In a study of patients with no history of atrial fibrillation or of stroke who had pacemakers or defibrillators implanted, Healey et al.[20] found that the presence of transient subclinical episodes of atrial tachyarrhythmia (>190/min, lasting >6 minutes) i.e., intermittent AF, recorded during a 3 month period following implantation predicted the occurrence of a stroke or other thromboembolic event during a followup period of 2.5 years, with 4.2%, 1.69%/year, having events, significantly greater than the 1.7%, 0.69%/year among the patients who did not have atrial tachyarrhythmias during the first 3 months (p=.007).

Our studies support those previously reported and have demonstrated that the stroke risk factors influence the occurrence of AF in these patients with ischemic stroke. The availability of ECGs taken over a long period of time have enabled us to diagnose intermittent AF in more stroke patients and to document the importance of AF as a very common factor in the etiology of ischemic stroke. Moreover, because we did not only study patients

with implanted pacemakers or AICDs, but studied routine stroke patients, the fact that patients with devices do not have normal hearts and the presence of a device that itself might induce AF, does not compromise the extrapolation of our findings to the usual stroke population.

The limitations of the current study are that it was retrospective and depended on the fortuitous recording of an ECG when the patient had AF. We also did not assess the incidence of AF in patients with similar risk factor demographics who did not have a stroke. The finding of AF was largely serendipitous and depended to a great extent on how often ECGs were recorded. Elderly patients and patients with CHF or CAD would be expected to have interface with the hospital more often with more ER visits and more admissions and hence the likelihood of recording intermittent AF would be greater. However, this error would suggest that the true incidence of AF in these stroke patients is higher than reported here. Future prospective studies should include using the presence of risk factors to determine which patients with cryptogenic stroke should be monitored for a long period of time.

Conclusions:

Because intermittent atrial fibrillation or flutter can play a role in ischemic stroke and is frequently not diagnosed, we have reviewed the clinical data and all the 12 lead ECGs in a 14 year institutional data base of 985 patients who had an ischemic stroke during a 3 year period and correlated the incidence of AF with the presence of the clinical stroke risk factors and with echocardiographic findings.We found a high incidence of AF in stroke patients with heart failure (62%), with advanced age (45%), with coronary disease (43%), with diabetes (39%), with hypertension (34%) or with left atrial enlargement (47%).Patients with 2 of these risk factors had a higher incidence of AF, approaching or exceeding 50%. We have also documented the value of using the longterm ECG data base available in many medical centers to diagnose intermittent AF in ischemic stroke patients.

Our studies suggest that AF is commonly found in patients with ischemic stroke who have the clinical risk factors for stroke and AF may be the common mechanism whereby the stroke risk factors, which are also risk factors for AF, cause stroke. The presence of more than one of these risk factors or the addition of left atrial enlargement justifies longterm monitoring to diagnose AF in patients with ischemic stroke who are in sinus rhythm. In the future when longterm monitoring to diagnose intermittent AF becomes more easily available, monitoring patients with multiple stroke risk factors who have not yet had a stroke might conceivably be performed so anticoagulation can be considered to prevent a first stroke.

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