New atrial fibrillation diagnosed by 30-day rhythm monitoring

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Background Recent studies of patients with pacemakers and implantable cardioverter/defibrillators have shown that subclinical atrial fibrillation (AF) is common and is associated with thromboembolic risk. We sought to evaluate the frequency, characteristics, and impact of new AF diagnosed by ambulatory 30-day rhythm monitoring.

Methods The 30-day rhythm monitoring data from January 2010 to August 2015 at our institution were reviewed. Medical record review was performed on patients that had a new or preexisting diagnosis of AF.

Results Of 2,326 patients without a previous diagnosis of AF, 78 had a new diagnosis of AF (3.4%) during 30-day monitoring. Patients with a new diagnosis of AF (mean age of 68.5 years, 56% female) had a mean CHA_2DS_2-VASc score of 3.2 (±1.8). The median time to diagnosis was 6 days, and 86% were diagnosed within 14 days. In 31 patients (40%), AF was exclusively detected automatically by the monitor. Of 46 patients that had manually activated the monitor, 34 also had automatically detected AF. Each patient had a median of 7 episodes, with the median duration of the longest episode being approximately 2 hours. Following the diagnosis of AF, 37 (47%) were started on anticoagulation and 9 (12%) were prescribed aspirin.

Conclusions A total of 3.4% of patients who underwent 30-day rhythm monitoring for any indication were found to have a new diagnosis of AF (402 per 1000 patient-years). Most of these episodes were detected automatically, corresponding to device-detected subclinical AF. The most common intervention following diagnosis of AF was initiation of oral anticoagulation. (Am Heart J 2019;209:29-35.)

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and has been estimated to affect >5 million Americans as of 2010.[1,2] This number is anticipated to rise to >12 million in 2030. The estimated incidence of AF in patients >65 years is about 28 per 1000 person-years.[3] Data from patients with pacemakers and implantable cardioverter/defibrillators (ICDs) suggest that traditional techniques of symptom-driven evaluation and random monitoring may underestimate the true prevalence of AF.[4] AF is known to increase the risk of stroke up to 5-fold and the risk of mortality up to 2-fold.[5] Much of device-detected AF is asymptomatic but is still associated with thromboembolic risk.[6,7]

Ambulatory cardiac rhythm monitoring is being increasingly used in multiple clinical scenarios.[8] Technological advances have allowed continuous ambulatory rhythm monitoring for up to 30 days, with automatic detection of arrhythmias, in addition to capturing the rhythm during symptoms by patient-triggered activation of the monitor.[9] In patients with cryptogenic stroke, 30-day monitoring has been shown to increase the yield of detecting AF.[10] We sought to evaluate the yield of detecting new AF in ambulatory patients undergoing routine 30-day monitoring for arrhythmias.

Methods

This retrospective observational study was approved by the Institutional Review Board of the University of Alabama at Birmingham. The results of all 30-day cardiac rhythm monitoring data using LifeWatch monitors (LifeWatch Services, Inc, Rosemont, IL) from January 2010 through August 2015 at our institution were reviewed. These monitors are classified as intermittent external patient- or event-activated recorders (external loop recorders) as described in section 3.1.3 of the 2017 Heart Rhythm

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Society and International Society for Holter and Noninvasive Electrocardiography (HRS-ISHNE) expert consensus statement on ambulatory ECG and external cardiac monitoring/telemetry.[11] Detailed medical record review was performed on every patient that had at least 1 episode of AF identified by 30-day monitoring. Patients found to have a preexisting diagnosis of AF or atrial flutter were examined separately. Patients with a new diagnosis of AF during the monitoring period underwent a thorough review of cardiology and primary care clinic notes, any procedure or hospital-based notes, and tracings from the monitor data. All ambulatory rhythm monitoring reports at our institution are reviewed by a board-certified cardiologist prior to finalization. The authors' review of the rhythm reports agreed with final diagnoses in all cases.

A diagnosis of AF or regular atrial tachyarrhythmia (ATA) was made when documented AF or ATA lasted greater than 1 minute. We defined regular atrial tachyarrhythmia as a documented regular atrial rate greater than 200 beat/min. The following were considered to be significant diagnoses during rhythm monitoring: AF, atrial tachyarrhythmia, pause greater than 3 seconds, bradycardia less than 30 beat/min, second-degree Mobitz II AV block, complete AV block, and wide complex tachycardia or ventricular tachycardia faster than 180 beat/min and lasting longer than 5 seconds.

The indication used for each monitor was gleaned from the clinical documents immediately preceding the monitor order or the order itself. Patient compliance in wearing the monitor was reviewed. Compliance was reported in 6-hour blocks.

All AF episodes were classified as patient triggered (manual) or automatically triggered (auto). AF burden was analyzed by reviewing the total number of AF episodes, the total percent time in AF, and the detailed breakdown regarding the length of each episode of AF if available. CHA_2DS_2-VASc score was calculated using the clinical encounter note immediately preceding the monitoring period.

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Results

Of 2,666 monitor records that were obtained (mean age of 60.2 years., 62% female), 423 revealed at least 1 episode of AF during the 30-day period. A total of 340 of these were in patients with a known diagnosis of AF or atrial flutter and were examined separately. Of the remaining 2,326 patients, 78 (3.4%) had an episode of AF lasting longer than 5 minutes. The characteristics of these patients are outlined in Table I. The mean CHA_2DS_2-VASc score of these patients was 3.2 (±1.8), with 80% having a CHA_2DS_2-VASc score of ≥2 (Figure 1).

Table I. Patient characteristics

Variable	New AF n = 78
Age	68.5 ± 10.9
Male	34 (43.5)
CHA_2DS_2-VASc score	3.2 ± 1.8
Risk factors	
Heart failure*	12 (15.4)
HTN	61 (78.2)
DM	18 (23.1)
CVA/TIA	5 (6.4)
Vascular disease	24 (30.7)
CAD	20 (25.6)

Data are shown as mean ± SD or n (percentage). *HTN*, hypertension; *DM*, diabetes mellitus; *CVA*, cerebrovascular accident; *TIA*, transient ischemic attack; *CAD*, coronary artery disease.
*One patient had an ejection fraction of 30%-35%. All remaining patients had an ejection fraction >40%.

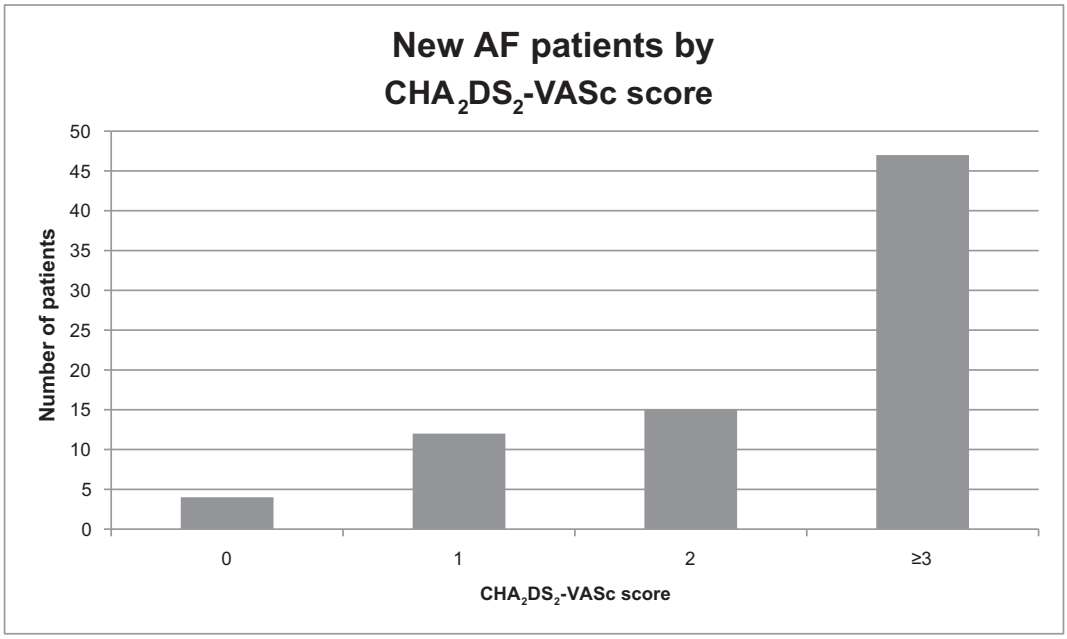
There were 340 patients with known AF who underwent event monitoring. Nineteen of these patients had more than 1 monitoring period, so for this analysis, the first monitoring period was analyzed. Of the 321 remaining patients with known AF, 77 did not have AF during this monitoring period. Detailed analysis was performed on the 244 remaining patients.

Seventy-seven patients (99%) with new AF had detailed information regarding the date of each episode. Of these patients, the median time to a significant diagnosis was 6 days. AF was the first significant diagnosis in all but 1 patient. Twenty-five patients had a diagnosis of ATA in addition to AF. Seven of 77 patients (9%) had a second significant diagnosis other than AF or ATA. The median time to the second diagnosis was 15.5 days. No patient had more than 2 significant diagnoses. The earliest diagnosis of AF was on day 1, and the latest diagnosis was on day 30. Forty-three patients (55.8%) had new AF diagnosed within 7 days, 54 (70.1%) within 10 days, and 66 (85.7%) within 14 days (Figure 2). The other significant diagnoses were ventricular tachycardia in 3 patients and pauses longer than 3 seconds in 4 patients.

The most common indication for ordering the event monitor in patients diagnosed with new AF was palpitations (43 patients, 55.1%), followed by syncope (9 patients, 11.5%), dizziness (6 patients, 7.7%), TIA (6 patients, 7.7%), and multiple or other indications in the remaining patients. The most common indications in the remaining patients mirrored this list: palpitations (35.5%), AF (26.3%), syncope (17.6%), dizziness (3.6%), and TIA (3.6%).

Patients with a new diagnosis of AF were fairly compliant with the monitor, wearing it a mean of 81.3% of the time prescribed (range 3.3%-100%). Twenty patients (25.6%) wore the monitor 100% of the time prescribed. An additional 25 patients (32.1%) wore the monitor at least 90% of the time prescribed, and an

Figure 1



New AF patients by CHA_2DS_2-VASc score: 80% of new AF patients had a CHA_2DS_2-VASc score of >2.

additional 13 patients (16.7%) wore the monitor at least 80% of the time prescribed.

Patients with preexisting AF were similarly adherent with the monitor. These patients wore it a mean of 81.8% of the time prescribed (range 3.7%-100%). Sixty-three patients (26.25%) wore the monitor 100% of the time prescribed. An additional 60 patients (25%) wore the monitor at least 90% of the time prescribed, and an additional 38 (15.8%) patients wore the monitor at least 80% of the time prescribed.

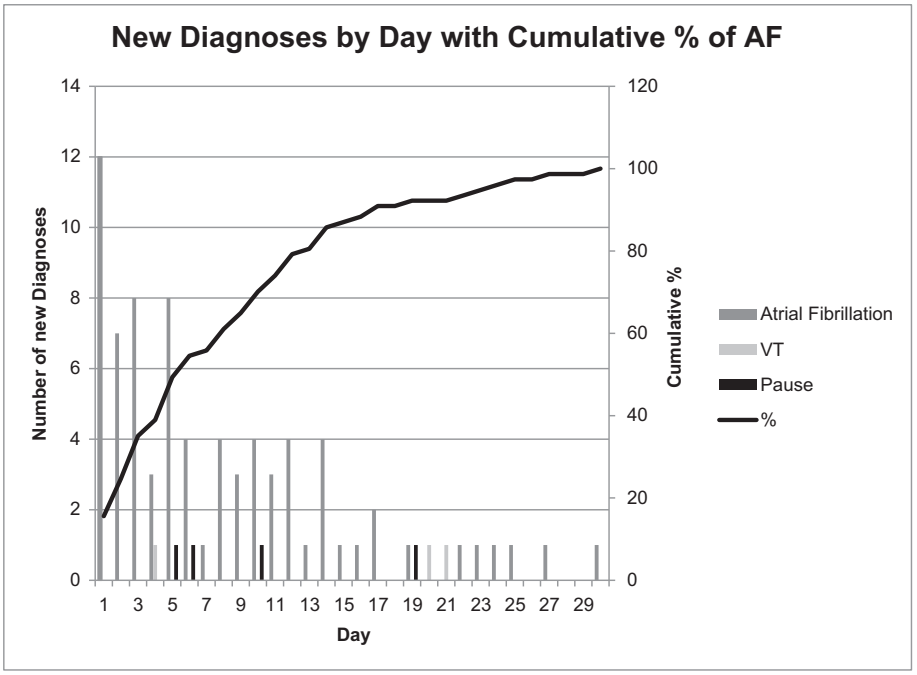
Seventy-seven patients (99%) had breakdown of manual versus automatically triggered events. In 31 of these (40%), there were no patient-triggered events, and AF was exclusively detected automatically by the monitor. In 12 patients (16%), all episodes of AF were manually triggered. Thirty-four patients (44%) had a combination of manually and automatically detected AF (Figure 3). In the 46 patients with manually triggered episodes of AF, several patient-triggered episodes were not associated with AF or other arrhythmias.

Seventy-seven patients (99%) had total number of episodes reported. The total number of AF episodes per patient ranged from 1 to 738, with a median of 7 (Figure 4). Of 73 patients (93.6%) in whom the percentage of time in AF was documented, the median time in AF was 1%, with a range of less than 1% to 100%. Thirty patients (4%) were in AF less than 1% of the time measured, which was the most frequently reported percentage. Individual episode duration was documented in 49 patients (63%) and ranged from 5 minutes and 34 seconds to greater than 63 hours. The median duration of the longest episode was 2 hours, 3 minutes, and 33 seconds. Forty-eight of 49 patients (98%) had at least 1 episode lasting longer than 6 minutes, and 14 of 49 patients (29%) had at least 1 episode lasting longer than 5.5 hours (Figure 5).

Of the 240 patients with preexisting AF, 233 (97%) had the total number of episodes reported. The total number of AF episodes per patient ranged from 1 to 1930, with a median of 17 (Figure 4). Of the 176 (73%) patients with percentage of time in AF documented, the median time in AF was 4%, with a range of less than 1% to 100%. Longest-episode duration was reported in 202 patients. The range was 60 seconds to greater than 142 hours. The median duration of the longest episode was 6 hours, 3 minutes, and 54 seconds. One hundred eighty-four of 202 patients (91%) had at least 1 episode lasting longer than 6 minutes, and 103 of 202 patients (51%) had at least 1 episode lasting longer than 5.5 hours (Figure 5).

Following the diagnosis of AF, 37 patients (47%) were started on anticoagulation (warfarin, 15; novel anticoagulants, 22), and 9 patients (12%) were prescribed aspirin. Twenty-three patients (29%) had rate control medications prescribed or adjusted, and 15 (21%) had rhythm control medications added. Fifteen patients (19%) had no changes to their previous regimen (including 3 that were already anticoagulated for other indications). Five patients (6%) underwent ablation following diagnosis.

Figure 2



New diagnoses by day with cumulative percentage of new AF diagnoses. The x-axis plots each day of the monitoring period. The y-axis shows the number of new diagnoses by day. AF = dark gray; ventricular tachycardia = light gray. Pause (black) denotes a pause greater than 3 seconds. The line graph superimposed on the chart shows the cumulative percentage of new AF diagnoses by day. *VT,* ventricular tachycardia.

Discussion

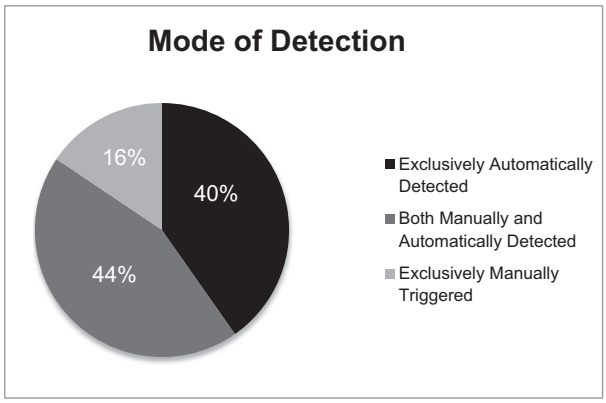
This study showed that 3.4% of patients who underwent 30-day rhythm monitoring for any indication were found to have a new diagnosis of AF. Many of the episodes of AF were detected automatically, corresponding to device-detected subclinical AF. The most common change in management following the diagnosis of new AF was initiation of oral anticoagulation.

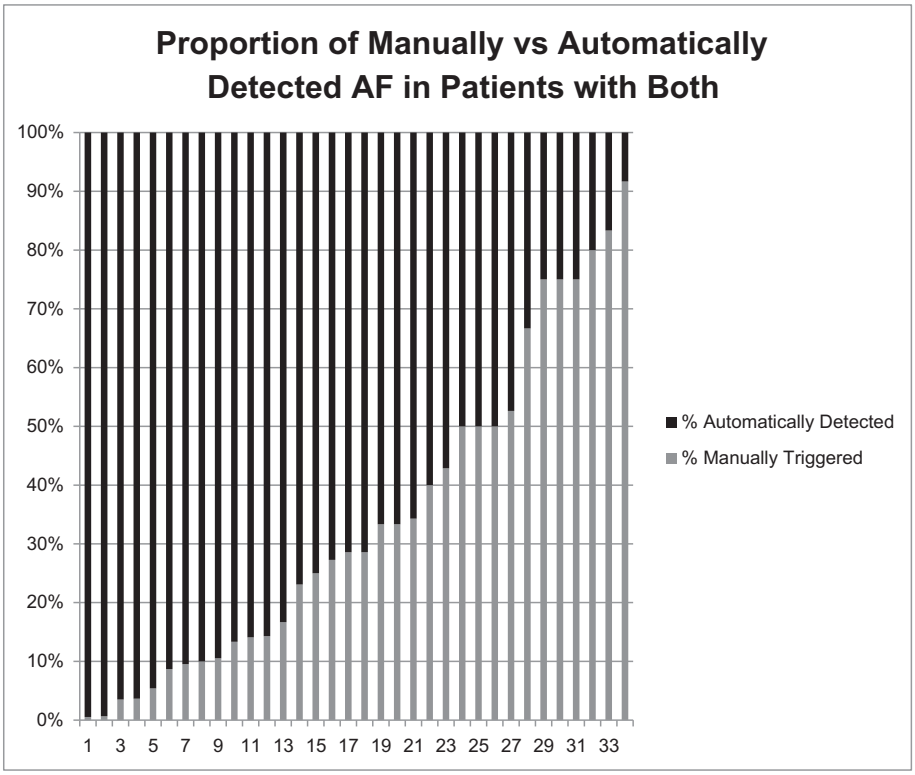
Emerging data from patients with pacemakers and ICDs reveal that AF is often subclinical and more prevalent than previously estimated.[6,7,12] The TRENDS study found that 891 of 1,988 patients (45%) with pacemakers or defibrillators had a new diagnosis of AF over 1.4 years.[6] In the ASSERT trial, 261 of 2,580 patients with pacemakers or ICDs (10.1%) had newly diagnosed AF by 3 months, whereas a total of 894 (34.6%) had this diagnosis over 2.5 years. In patients with cryptogenic stroke, longer durations of rhythm monitoring using 30-day monitors or implantable cardiac monitors have shown a higher yield of detecting AF compared to traditional shorter monitoring techniques.[10,13] In the EMBRACE trial, AF lasting more than 30 seconds was diagnosed in 45 of 280 patients (16.1%) with recent cryptogenic stroke by 30-day rhythm monitoring.[10] Using an implantable cardiac monitor in patients with cryptogenic stroke, the CRYSTAL AF study found AF in 8.9% of patients by 6 months, in 12.4% by 12 months, and in 30% by 36 months.[13] Of note, patients with dual-chamber pacemakers or ICDs and those with cryptogenic stroke would be expected to have a higher prevalence of AF than the general population. In our study, new AF was diagnosed in 3.6% of patients undergoing routine ambulatory 30-day monitoring, which is lower than that seen in patients with cryptogenic stroke over the same period in the EMBRACE trial but higher than that would be expected with routine clinical evaluation. Ongoing studies using implantable cardiac monitors (GRAF, ASSERT-II, REVEAL AF) or nonimplantable devices (SCREEN-AF, SEARCH-AF, etc) should provide insight into the incidence of subclinical AF in the general population and in those with risk factors for stroke.[14]

In 40% of patients in our study, all episodes of AF were automatically detected, corresponding to subclinical AF. In the patients that had manually triggered AF, there was poor correlation between patient-triggered recordings and AF. Additionally, approximately one-third of the patients with new AF underwent rhythm monitoring for indications other than palpitations or suspected AF, underscoring the fact that routine clinical evaluation would not have detected most of these episodes of AF.

Incidentally detected episodes of AF have been shown to be associated with thromboembolic risk as a function of AF burden.[6,7] The advent of continuous monitoring through implanted devices has allowed precise

Figure 3

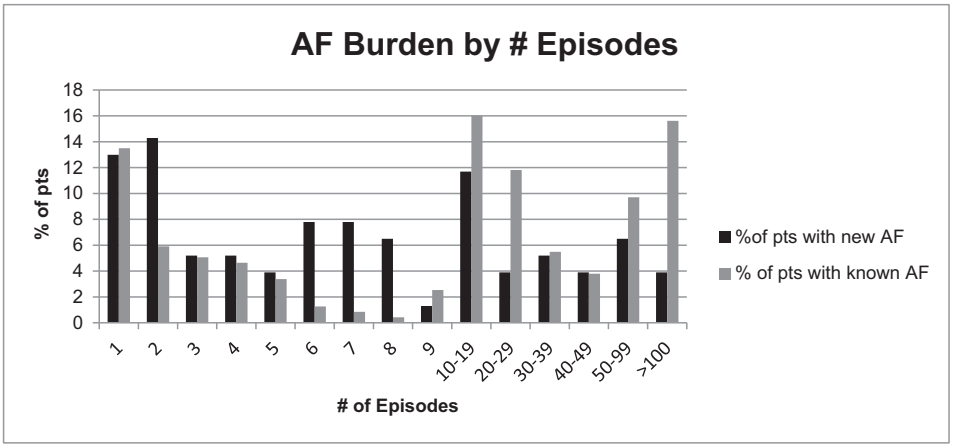




AF by mode of detection. **A**, The percentage of patients in whom AF was detected exclusively automatically, always manually triggered by the patient, or detected both automatically and manually. **B**, The proportion of patient triggered and automatically detected AF episodes in patients that had both types of episodes, with increasing proportion of manually detected episodes from right to left.

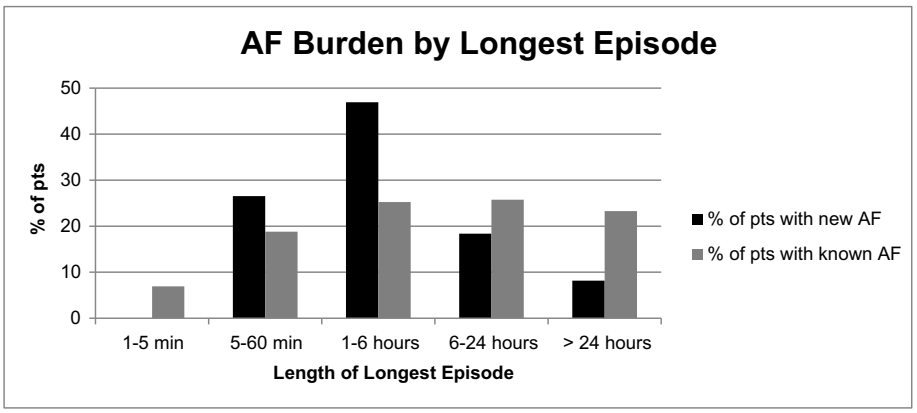
estimation of AF burden. The TRENDS study showed that AF lasting greater than 5.5 hours on any given day in the past 30 days doubled the risk of thromboembolic events compared to lower-duration or no AF.[6] The ASSERT trial showed that patients with more than 6 minutes of AF had a higher thromboembolic risk compared to those without this finding.[7] In our study, 100% of patients with a new diagnosis of AF had at least 1 episode lasting longer than 5 minutes and 29% had at least 1 episode lasting longer than 5.5 hours, suggesting that these are clinically significant diagnoses. Combining CHA_2DS_2-VASc score with AF burden has been shown to improve thromboembolic risk

Figure 4



AF burden by total number of episodes per patient.

Figure 5



AF burden by duration of longest episode.

stratification.[15] Eighty percent of patients with newly diagnosed AF in our study had a CHA2DS2-VASc score of >2, suggesting an elevated risk of thromboembolic events.

It is well known that oral anticoagulation decreases the risk of stroke in clinical AF.[5] There are no published studies of oral anticoagulation in subclinical AF. Ongoing trials include the Apixaban for the Reduction of Thrombo-Embolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation (ARTESiA) trial and the Non-vitamin K Antagonist Oral Anticoagulants in Patients with Atrial High Rate Episodes (NOAH) trial. In our study, oral anticoagulation was initiated in 47% of patients following diagnosis of new AF. A similar pattern was observed in the CRYSTAL AF and the EMBRACE trials, both of which showed increased utilization of oral anticoagulation following diagnosis of new AF in patients with cryptogenic stroke.[10,13]

Conclusion

Routine clinical evaluation underestimates the incidence and prevalence of AF. This study found that new AF was identified in 3.4% of patients undergoing 30-day rhythm monitoring for various indications. Most of these

episodes were automatically detected, corresponding to subclinical AF. Because of the paucity of literature, clinicians must manage these patients based on extrapolated data from similar yet different populations or use clinical gestalt. Further research is needed to determine the best management practices for these patients.

References

1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. Circulation 2016;133:e38-e360.
2. Colilla S, Crow A, Petkun W, et al. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. Am J Cardiol 2013;112:1142-7.
3. Piccini JP, Hammill BG, Sinner MF, et al. Incidence and prevalence of atrial fibrillation and associated mortality among Medicare beneficiaries, 1993-2007. Circ Cardiovasc Qual Outcomes 2012;5:85-93.
4. Ziegler PD, Glotzer TV, Daoud EG, et al. Detection of previously undiagnosed atrial fibrillation in patients with stroke risk factors and usefulness of continuous monitoring in primary stroke prevention. Am J Cardiol 2012;110:1309-14.
5. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med 2007;146:857-67.
6. Glotzer TV, Daoud EG, Wyse DG, et al. The relationship between daily atrial tachyarrhythmia burden from implantable device diagnostics and stroke risk: the TRENDS study. Circ Arrhythm Electrophysiol 2009;2:474-80.
7. Healey JS, Connolly SJ, Gold MR, et al. Subclinical atrial fibrillation and the risk of stroke. N Engl J Med 2012;366:120-9.
8. Giada F, Bartoletti A. Value of ambulatory electrocardiographic monitoring in syncope. Cardiol Clin 2015;33:361-6.
9. Fung E, Jarvelin MR, Doshi RN, et al. Electrocardiographic patch devices and contemporary wireless cardiac monitoring. Front Physiol 2015;6:1-10.
10. Gladstone DJ, Sharma M, Spence JD. Investigators ESCa. Cryptogenic stroke and atrial fibrillation. N Engl J Med 2014;371:2478--2486.
11. Steinberg JS, Varma N, Cygankiewicz I, et al. 2017 ISHNE-HRS consensus statement on ambulatory ECG and external cardiac monitoring/telemetry. Ann Noninvasive Electrocardiol 2017;22, e12447.
12. Miyasaka Y, Barnes ME, Bailey KR, et al. Mortality trends in patients diagnosed with first atrial fibrillation: a 21-year community-based study. J Am Coll Cardiol 2007;49:986-92.
13. Sanna T, Diener HC, Passman RS, et al. Cryptogenic stroke and underlying atrial fibrillation. N Engl J Med 2014;370:2478-86.
14. Hess PL, Healey JS, Granger CB, et al. The role of cardiovascular implantable electronic devices in the detection and treatment of subclinical atrial fibrillation: a review. JAMA Cardiol 2017;2:324-31.
15. Botto GL, Padeletti L, Santini M, et al. Presence and duration of atrial fibrillation detected by continuous monitoring: crucial implications for the risk of thromboembolic events. J Cardiovasc Electrophysiol 2009;20:241-8.