


openheart Prediction of atrial fibrillation using a home blood pressure monitor with a high-resolution system

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ABSTRACT

Objective The usefulness of screening for atrial fibrillation (AF) using several home blood pressure (BP) monitors has been reported. We evaluated the accuracy of a high-resolution system (HiRS) for AF prediction and its usefulness when installed in home BP monitors.

Methods In patients with paroxysmal, persistent or permanent AF, ECG recording and BP measurements were performed simultaneously. The relationship between ECG rhythm diagnosis and pulse irregularity recognition, using a home BP monitor with HiRS, was investigated. The severity of a pulse disturbance during BP measurement was displayed as an irregular pulse rhythm symbol (IPRS) in three instances. The IPRS was not displayed if the pulse was regular, turned on if there was a weak variation in the pulse, and blinked if there was a strong variation in the pulse.

Results One hundred and seven patients (44 paroxysmal AF, 63 persistent or permanent AF) were enrolled, and a total of 333 recordings were analysed. The rhythms recorded by each ECG were 73 sinus regular rhythms, 35 extrasystoles, 222 AFs and 3 atrial flutters. Sensitivity and specificity for the prediction of any arrhythmia by the IPRS display of the BP monitor were 95.8% (95% CI 92.6% to 97.6%) and 96.8% (95% CI 92.6% to 100%), respectively. In addition, sensitivity and specificity for the prediction of AF were 100% (95% CI 97.5% to 100%) and 74.8% (95% CI 65.6% to 82.5%), respectively. Sensitivity and specificity for the prediction of AF by the IPRS blinking display were 88.3% (95% CI 83.3% to 92.2%) and 94.6% (95% CI 88.6% to 98.0%), respectively. IPRS exhibited lighting or blinking during AF occurrence; however, during sinus rhythm, IPRS was not displayed in 72 out of 73 recordings.

Conclusion The IPRS device predicted AF with precision and may be particularly useful for predicting an arrhythmia attack in patients with paroxysmal AF.

INTRODUCTION

The frequency of atrial fibrillation (AF) associated with ischaemic stroke instances is approximately 20%–30%,^{1–3} which is thought to include asymptomatic AF. It has also been reported that 37.5% of paroxysmal AF detected is asymptomatic.⁴ Therefore, detecting asymptomatic AF is one of the main problems hindering treatment. As a method for predicting the possibility of AF,

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ A home blood pressure (BP) monitor (Microlife Watch BP Home A) was recommended by the UK National Institute for Heart and Care Excellence to screen for atrial fibrillation. Many studies have examined the accuracy of several devices for atrial fibrillation detection but there is a need for a sensitive and reliable system.

WHAT THIS STUDY ADDS

⇒ The accuracy of predicting atrial fibrillation by this home BP monitor with the high-resolution system (HiRS; NISSEI WS-X10J) software is demonstrated in this study.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This home BP monitor with the HiRS will be useful for the management of atrial fibrillation attacks in patients who will then be prompted to visit medical institutions and seek treatment.

many studies have reported AF screening using home blood pressure (BP) monitors.^{5–14} The UK National Institute for Heart and Care Excellence recommends the use of a home BP monitor (Microlife WatchBP Home A) for detecting AF during the diagnosis and monitoring of hypertension.¹⁵ However, a device with higher precision is necessary and to date, the usefulness of a home BP monitor for patients diagnosed with paroxysmal AF has not been reported. We investigated the accuracy for AF prediction by the high-resolution system (HiRS), which is a high-precision pulse wave interval measurement system and developed for detecting AF by enhancing the irregular pulse sensing ability installed in home BP monitor and evaluated its significance in patients with paroxysmal AF.

METHODS

Patients

In this study, we examined outpatients and inpatients who presented AF at least once on



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an ECG at the Ebara hospital, Tokyo, Japan. We excluded patients with implanted pacemakers or implantable cardioverter-defibrillators (ICDs), patients who did not consent to participate in the study and patients with dementia who were deemed inappropriate by their doctors because they were unable to understand the purpose of the study.

Procedures

Clinical laboratory technicians recorded a standard 12-lead ECG and a single lead II ECG for each patient at rest, for 3 min, using an electrocardiograph (Nihon Kohden, Tokyo, Japan). Simultaneously, BP was measured using a wrist-type digital BP monitor (NISSEI WS-X10J, Nihon Seimitsu Sokki, Gunma, Japan) every min. The measurements were recorded in triplicate, but each data set was analysed independently. The NISSEI WS-X10J is equipped with a high-precision pulse wave interval measurement system, namely a HiRS. The disturbance of a pulse during BP measurement was displayed as an irregular pulse rhythm symbol (IPRS) in three instances. That is, IPRS was not shown when the pulse wave intervals were regular. However, IPRS was displayed as 'lighting' for a weak variation in the pulse wave intervals and as 'blinking' when a strong variation was detected.

Therefore, IPRS was recorded as either hidden, lighting or blinking for each measurement.

A cardiologist performed a minute-by-minute ECG rhythm diagnosis, and the relationship between the ECG diagnosis results and the IPRS display was examined. Since it is necessary for the BP monitor to accurately capture the pulse in order to recognise the variation in the pulse, the consistency between the heart rate (HR), calculated by ECG, and the pulse rate (PR) determined by the BP monitor was evaluated in this study. In addition, since systolic BP may be decreased in AF, we compared systolic BP during sinus rhythm and AF.

Statistics

Sensitivity, specificity, positive likelihood ratio, negative likelihood ratio and accuracy were calculated from the 2×2 contingency table. Linear regression analysis and Pearson correlation coefficients were used to assess the relationship between HR and PR. Differences between continuous variables including systolic BP at sinus rhythm and AF were analysed with a Student's *t*-test. All statistical analyses were performed with EZR software (Easy

R; Saitama Medical Centre, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R and R commander and is designed to add statistical functions frequently used in biostatistics.¹⁶ Statistical significance was defined as a probability (*p*) value of <0.05.

RESULTS

In total, 107 subjects (70 males, 37 females; average age 77.0±8.4 years) that included 44 paroxysmal AF cases, and 63 persistent or permanent AF cases were assessed in this study. In most cases of permanent AF, patients were unaware of their arrhythmias. In addition, paroxysmal AF cases also included asymptomatic patients. The characteristics of these patients included hypertension (68.9%), diabetes (34.9%), heart failure (13.2%), stroke history (13.2%) and coronary artery disease history (18.9%). For each case, an ECG was recorded for 3 min and BP was measured every min. These results were analysed with a total of 333 recordings. Four cases with paroxysmal AF were examined during AF and non-AF. The ECG rhythm diagnoses per minute performed at the same time as that of the BP measurements were 73 regular sinus rhythm, 35 extrasystole, 222 AF and 3 atrial flutter. While IPRS was not apparent in 72/73 regular sinus rhythm recordings, IPRS was displayed in AF cases. Moreover, IPRS was not displayed in three atrial flutter cases because the RR intervals were constant. IPRS lighting patterns were more frequent than blinking displays in extrasystoles and blinking was observed more frequently than lighting in AF (table 1).

The prediction of any arrhythmia by IPRS display showed a 95.8% (95% CI 92.6% to 97.6%) sensitivity and 96.8% (95% CI 92.6% to 100%) specificity. In addition, the prediction of AF by IPRS display was 100% (95% CI 97.5% to 100%) and 74.8% (95% CI 65.6% to 82.5%) sensitive and specific, respectively (table 2). The prediction of AF by a blinking IPRS display showed 88.3% (95% CI 83.3% to 92.2%) sensitivity and 94.6% (95% CI 88.6% to 89.0%) specificity (table 3).

The association between HR, determined by ECG and the PR, measured using a BP monitor, at sinus rhythm and AF was evaluated. A positive correlation was obtained between HR and PR with *r*=0.965 (95% CI 0.941 to 0.98) and *r*=0.873 (95% CI 0.837 to 0.901) during sinus rhythm

Table 1 IPRS display and blood pressure in each rhythm

ECG diagnosis	No	IPRS not displayed	IPRS lighting	IPRS blinking	Systolic BP (mm Hg)	Diastolic BP (mm Hg)
Sinus rhythm	73	72	1	0	127.7±17.8	72.3±11.9
Extrasystole	35	8	21	6	129.0±17.2	73.1±10.3
AF	222	0	26	196	123.6±17.0	73.5±14.5
AFI	3	3	0	0	133.3±7.1	71.7±3.2

AF, atrial fibrillation; AFI, atrial flutter; BP, blood pressure; ECG, electrocardiogram; IPRS, irregular pulse rhythm symbol.

Table 2 2x2 contingency tables for arrhythmia and atrial fibrillation cases

A	Arrhythmia	Non-arrhythmia	Total
IPRS (Lighting or blinking)	249	1	250
IPRS (not displayed)	11	72	83
	260	73	333
B	AF	Non-AF	Total
IPRS (Lighting or blinking)	222	28	250
IPRS (not displayed)	0	83	83
	222	111	333

(A) Prediction of any arrhythmia by IPRS, (B) Prediction of atrial fibrillation by IPRS.
AF, atrial fibrillation; IPRS, irregular pulse rhythm symbol.

and AF, respectively. However, variation in rapid AF was observed (figure 1). We compared systolic BP during sinus rhythm and AF. Systolic BP during AF was marginally lower than during sinus rhythm, but there was no significant difference between the two groups (127.7 ± 17.8 mm Hg vs 123.6 ± 17.0 mm Hg, $p=0.07$; table 1).

DISCUSSION

Non-invasive medical tools for detecting AF, either symptomatic or non-symptomatic, include the standard ECG, the 24-hour or the long-term digital Holter ECG monitoring system. It is known that the longer the monitoring time, the higher the AF detection ability. Continuous monitoring tools include pacemakers, intracardiac defibrillators and intracardiac monitors. Subclinical atrial tachyarrhythmias were detected frequently by implanted pacemakers and were found to be associated with a significantly increased risk of ischaemic stroke or systemic embolism.¹⁷ In addition, the usefulness of intracardiac monitors in patients with cryptogenic stroke has been reported.^{18–20} However, these devices were implanted through invasive methods for limited indication. Furthermore, the detection of AF using general health devices and wearable devices has been actively attempted,^{21–24}

Table 3 Diagnostic values for atrial fibrillation by irregular pulse rhythm symbol blinking displays

Statistic	Value	95% CI
Sensitivity	88.3%	83.3% to 92.2%
Specificity	94.4%	88.6% to 98.0%
PPV	97.0%	93.6% to 98.9%
NPV	80.2%	72.3% to 86.6%
Accuracy	90.4%	86.7% to 93.3%
PLR	16.333	7.490 to 35.620
NLR	0.124	0.086 to 0.178

NLR, negative likelihood ratio; NPV, negative predictive value; PLR, positive likelihood ratio; PPV, positive predictive value.

including a home BP monitoring system. These methods have advantages and disadvantages in terms of adaptability, expense, convenience, operability for the elderly and accuracy, among others. The home BP monitor is not a continuous monitor and cannot directly record AF. However, it has the advantage of being a relatively inexpensive device that is excellent in operability for the elderly, it is uncomplicated to read the results, and can determine daily BP. The device used in this study was a model with an enhanced AF prediction function, and its accuracy and significance were evaluated.

A significant feature of the HiRS is to accurately recognise pulse irregularity, and this model showed good results. That is, the specificity of any arrhythmia detection was 98.6%, and when IPRS was displayed, extrasystoles or AF were observed during the BP measurements, except once. This device may be used to warn patients to visit a hospital for arrhythmia screening or suspected paroxysmal AF. Sensitivity for the prediction of AF with IPRS display was 100%. If the IPRS was not displayed, AF was not detected. This may be very valuable to patients with paroxysmal AF, especially asymptomatic AF cases. Furthermore, sensitivity of IPRS blinking displays for AF prediction was 88% and the specificity was 94% rendering it a powerful indicator of suspected AF. When IPRS is displayed, extrasystole or AF may be occurring. In particular, an IPRS blinking display, strongly coincides with possible AF and warrants a consultation with a medical expert.

In several clinical trials, the accuracy for AF detection, using numerous BP monitors, was determined by sensitivity and specificity that ranged from 0.83 to 1.00 and from 0.85 to 98.7, respectively. These studies evaluated three BP measurements to improve accuracy.^{4 9–11 23 25} The BP monitor of the current study was equipped with HiRS which resulted in high accuracy and usefulness using one BP measurement (table 4).

It has been reported that supraventricular extrasystoles are a risk factor for AF.^{26 27} Therefore, the display of IPRS due to frequent extrasystoles is considered a precursor for AF and should be treated in the same way as AF.

For AF (absolute arrhythmia), the pulse interval and intensity vary from beat to beat. Therefore, the question arises as to how reliable the PR, determined by a sphygmomanometer, is. With the home BP monitor system, the PR is calculated from the average pulse interval. However, an ECG excludes cycle lengths with RR intervals of $\geq 20\%$ and calculates the HR. The HR calculated using an ECG and the PR by the sphygmomanometer showed a good correlation during regular sinus rhythm. But, this study has no data on the correlation between HR and PR in sinus tachycardia. Therefore, further studies are necessary to confirm the performance of the device in sinus tachycardia. The overall correlation between HR and PR during AF was good, $r=0.83$. However, a closer look only at rapid AF shows that PR does not follow HR. There are two possible reasons for this: first, the sampling period with the sphygmomanometer is shorter than with a 1 min

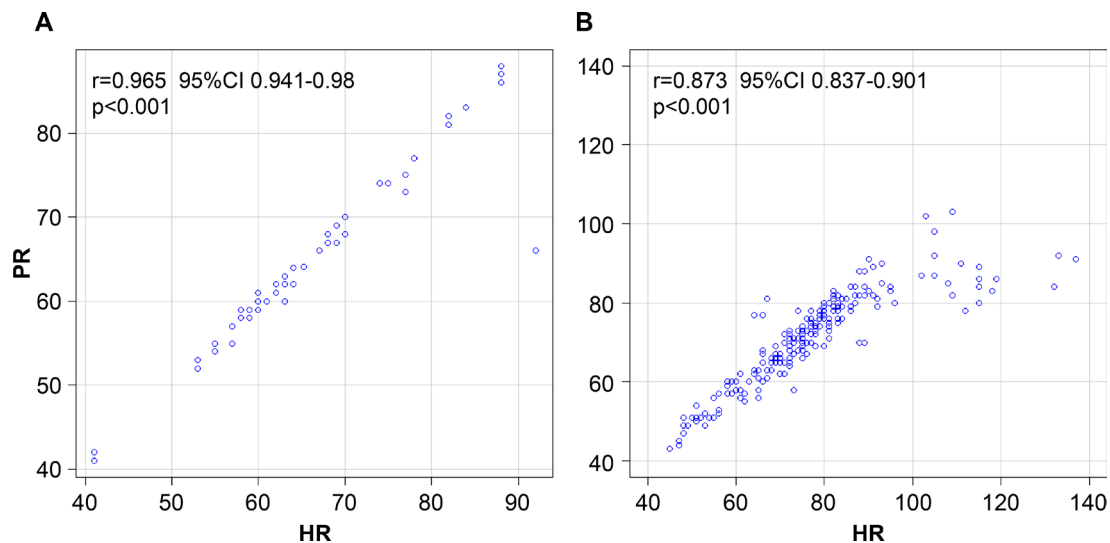


Figure 1 Relationship between heart rate (HR) determined using an ECG and pulse rate (PR) measured using a blood pressure monitor. (A) PR versus HR in sinus rhythm and (B) during atrial fibrillation.

ECG, and second, during rapid AF, pulse intensity fluctuations are greater, resulting in imperceptible pulses. The latter appears to be a limitation of the sphygmomanometer. Therefore, the ability to predict AF may be reduced in rapid AF. In practice, however, the ability to predict AF was not impaired because the pulse interval variability was still sufficiently significant, even in the presence of undetectable weak pulses.

Limitations

IPRS was displayed for 27 out of 35 patients with extrasystole. If one or more extrasystole was observed in the ECG recording for a minute, which contained inside and outside BP measurement time, then it was classified as an extrasystole group. On the contrary, the BP monitor requires 40–45s to measure BP, which will depend on the systolic BP value, and senses the pulse for 20–25s after approximately 20s of pressurisation initiation. Because the extrasystole outside the pulse sensing period could not be recognised by the BP monitor, the sensing ability of the HiRS for extrasystole was underestimated. Conversely, this study did not include patients with sinus arrhythmia or second-degree atrioventricular block. It is predicted that if such arrhythmia is present, the accuracy may decrease.

Future challenges

The overall preventive effect of direct oral anticoagulants (DOACs) for cerebral infarction or systemic embolism in AF patients is thought to outweigh the disadvantages.^{28–31} The European Society of Cardiology recommends oral administration of DOACs for their preventive effect in patients with AF who have a CHA₂DS₂-VASc score of ≥ 2 in males or ≥ 3 in females.¹ However, in individual cases, the advantages of DOACs do not always outweigh the disadvantages. The DOACs cannot completely prevent cerebral infarction or systemic embolism, may cause major bleeding and are expensive. The anticoagulant effect of the DOACs is highly necessary for persistent AF patients with a high embolic risk, but it is unnecessary during the stable sinus rhythm for paroxysmal AF patients, especially in low-frequency attacks. Persistent AF for >24hours in patients receiving a pacemaker or intracardiac defibrillator increased the risk of embolism.³² However, the burden and duration of paroxysmal AF cannot be predicted accurately without the use of continuous monitoring devices. If an AF occurrence can be accurately identified without the use of continuous monitoring implanted devices, then it may be possible to determine the appropriate time for administering

Table 4 Clinical trials assessing the diagnostic accuracy of atrial fibrillation detection by several blood pressure monitors

Study	Device	Sensitivity (%)	Specificity (%)	No of measurements
Wiesel <i>et al</i> (2009) ⁶	Microlife BP3MQ1-2D	96.8	88.8	3
Chan <i>et al</i> (2017) ¹²	Microlife WatchBP	83.3	98.7	3
Ishizawa <i>et al</i> (2019) ¹¹	Omron HEM-907	95.5	96.5	3
Balanis and Sanner (2021) ¹³	Omron BP785N	100	84.8	3
This study	NISSEI WS-X10J	100 (lighting/blinking), 88.0 (blinking)	74.8 (lighting/blinking), 93.1 (blinking)	1

DOACs ('pill-in-the-pocket' approach). To overcome the challenge, the optimal number of home BP monitor measurements for predicting AF efficiently requires investigation in the future.

CONCLUSION

The HiRS, as a high-precision pulse wave interval measurement system, was able to predict, with high accuracy, whether an AF attack occurred in a single measurement. The HiRS-equipped home BP monitor may be useful for predicting, not only symptomatic but also, asymptomatic AF.

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Data availability statement Data are available on reasonable request.

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REFERENCES

- Hindricks G, Potpara T, Dagres N, *et al.* 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European association of Cardio-Thoracic surgery (EACTS). *Eur Heart J* 2021;42:373–498.
- Sposato LA, Cipriano LE, Saposnik G, *et al.* Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis. *Lancet Neurol* 2015;14:377–87.
- Marini C, De Santis F, Sacco S, *et al.* Contribution of atrial fibrillation to incidence and outcome of ischemic stroke: results from a population-based study. *Stroke* 2005;36:1115–9.
- Esato M, Chun Y-H, An Y, *et al.* Clinical impact of asymptomatic presentation status in patients with paroxysmal and sustained atrial fibrillation: the Fushimi AF registry. *Chest* 2017;152:1266–75.
- Wiesel J, Wiesel D, Suri R, *et al.* The use of a modified sphygmomanometer to detect atrial fibrillation in outpatients. *Pacing Clin Electrophysiol* 2004;27:639–43.
- Wiesel J, Fitzig L, Herschman Y, *et al.* Detection of atrial fibrillation using a modified microlife blood pressure monitor. *Am J Hypertens* 2009;22:848–52.
- Stergiou GS, Karpettas N, Protogerou A, *et al.* Diagnostic accuracy of a home blood pressure monitor to detect atrial fibrillation. *J Hum Hypertens* 2009;23:654–8.
- Wiesel J, Abraham S, Messineo FC. Screening for asymptomatic atrial fibrillation while monitoring the blood pressure at home: trial of regular versus irregular pulse for prevention of stroke (TRIPPS 2.0). *Am J Cardiol* 2013;111:1598–601.
- Marazzi G, Iellamo F, Volterrani M, *et al.* Comparison of Microlife BP A200 plus and Omron M6 blood pressure monitors to detect atrial fibrillation in hypertensive patients. *Adv Ther* 2012;29:64–70.
- Wiesel J, Arbesfeld B, Schechter D. Comparison of the Microlife blood pressure monitor with the Omron blood pressure monitor for detecting atrial fibrillation. *Am J Cardiol* 2014;114:1046–8.
- Ishizawa M, Noma T, Izumi T, *et al.* Development of a novel algorithm to detect atrial fibrillation using an automated blood pressure monitor with an irregular heartbeat detector. *Circ J* 2019;83:2428–33.
- Chan P-H, Wong C-K, Pun L, *et al.* Head-To-Head comparison of the AliveCor heart monitor and Microlife WatchBP office AFIB for atrial fibrillation screening in a primary care setting. *Circulation* 2017;135:110–2.
- Balanis T, Sanner B. Detection of atrial fibrillation using a home blood pressure monitor. *Vasc Health Risk Manag* 2021;17:407–14.
- Chan P-H, Wong C-K, Pun L, *et al.* Diagnostic performance of an automatic blood pressure measurement device, Microlife WatchBP home a, for atrial fibrillation screening in a real-world primary care setting. *BMJ Open* 2017;7:e013685.
- Willits I, Keltie K, Craig J, *et al.* WatchBP home a for opportunistically detecting atrial fibrillation during diagnosis and monitoring of hypertension: a NICE medical technology guidance. *Appl Health Econ Health Policy* 2014;12:255–65.
- Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. *Bone Marrow Transplant* 2013;48:452–8.
- Healey JS, Connolly SJ, Gold MR, *et al.* Subclinical atrial fibrillation and the risk of stroke. *N Engl J Med* 2012;366:120–9.
- Sanna T, Diener H-C, Passman RS, *et al.* Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med* 2014;370:2478–86.
- Brachmann J, Morillo CA, Sanna T, *et al.* Uncovering atrial fibrillation beyond short-term monitoring in cryptogenic stroke patients: three-year results from the cryptogenic stroke and underlying atrial fibrillation trial. *Circ Arrhythm Electrophysiol* 2016;9:e003333.
- De Angelis MV, Di Stefano V, Franciotti R, *et al.* Cryptogenic stroke and atrial fibrillation in a real-world population: the role of insertable cardiac monitors. *Sci Rep* 2020;10:3230.
- Rajakariar K, Koshy AN, Sajeev JK, *et al.* Accuracy of a smartwatch based single-lead electrocardiogram device in detection of atrial fibrillation. *Heart* 2020;106:665–70.
- Proesmans T, Mortelmans C, Van Haelst R, *et al.* Mobile phone-based use of the photoplethysmography technique to detect atrial fibrillation in primary care: diagnostic accuracy study of the FibrCheck App. *JMIR Mhealth Uhealth* 2019;7:e12284.
- Brasier N, Raichle CJ, Dörr M, *et al.* Detection of atrial fibrillation with a smartphone camera: first prospective, international, two-centre, clinical validation study (DETECT AF PRO). *J Europace* 2019;21:41–7.
- Li KHC, White FA, Tipoe T, *et al.* The current state of mobile phone Apps for monitoring heart rate, heart rate variability, and atrial fibrillation: narrative review. *JMIR Mhealth Uhealth* 2019;7:e11606.
- Verberk WJ, de Leeuw PW. Accuracy of oscillometric blood pressure monitors for the detection of atrial fibrillation: a systematic review. *Expert Rev Med Devices* 2012;9:635–40.
- Binici Z, Intzilakis T, Nielsen OW, *et al.* Excessive supraventricular ectopic activity and increased risk of atrial fibrillation and stroke. *Circulation* 2010;121:1904–11.
- Wallmann D, Tüller D, Wustmann K, *et al.* Frequent atrial premature beats predict paroxysmal atrial fibrillation in stroke patients: an opportunity for a new diagnostic strategy. *Stroke* 2007;38:2292–4.
- Patel MR, Mahaffey KW, Garg J, *et al.* Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med* 2011;365:883–91.
- Connolly SJ, Ezekowitz MD, Yusuf S, *et al.* Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2009;361:1139–51.
- Giugliano RP, Ruff CT, Braunwald E, *et al.* Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2013;369:2093–104.
- Granger CB, Alexander JH, McMurray JJV, *et al.* Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2011;365:981–92.
- Van Gelder IC, Healey JS, Crijns HJGM, *et al.* Duration of device-detected subclinical atrial fibrillation and occurrence of stroke in ASSERT. *Eur Heart J* 2017;38:1339–44.