Circulation Reports
Circ Rep 2024; 6: 110–117
doi:10.1253/circrep.CR-24-0008

ORIGINAL ARTICLE
Arrhythmia/Electrophysiology

Diagnostic Performance of an Automated Blood Pressure Monitor With an Irregular Heartbeat Algorithm Designed to Detect Atrial Fibrillation

Yu Ishihara, MD; Makoto Ishizawa, MD, PhD; Takahisa Noma, MD, PhD; Minako Ohara, MD, PhD; Ryosuke Tani, MD; Genki Kurashita, MD; Yuta Toda, MD; Waki Kobayashi, MD; Tetsuo Minamino, MD, PhD

Background: Early detection of atrial fibrillation (AF) remains an unsolved challenge and because the greatest risk factor for AF is hypertension, blood pressure (BP) monitors with AF detectors have been developed. We evaluated the clinical performance of an irregular heartbeat (IHB) algorithm built into an A&D automated BP monitor for AF diagnosis.

Methods and Results: Each of the 239 enrolled patients underwent BP measurement 3 times using the A&D UM-212 with the IHB algorithm. Real-time 3-lead ECG was recorded using automated ECG analysis software. Independent of the ECG analysis software results, 2 cardiologists interpreted the ECG and made the final diagnosis. Of the 239 patients, 135 were in sinus rhythm, 31 had AF, and 73 had non-AF arrhythmias. The respective sensitivity, specificity, and accuracy of the IHB algorithm for AF diagnosis were 98.9%, 91.2%, and 92.2% for the per-measurement evaluation, and 96.8%, 95.7%, and 95.8% for the per-patient evaluation (3/3 positive measurements). The respective sensitivity, specificity, and accuracy of the ECG analysis software for AF diagnosis were 91.4%, 97.9%, and 97.1% for the per-measurement evaluation, and 77.4%, 99.5%, and 96.7% for the per-patient evaluation (3/3 positive measurements).

Conclusions: The IHB algorithm built into an A&D automated BP monitor had high diagnostic performance for AF in general cardiology patients, especially when multiple measurements were obtained.

Key Words: Analysis software; Atrial fibrillation; Automated blood pressure monitor; Electrocardiogram; Irregular heartbeat algorithm

One of the most common arrhythmias, atrial fibrillation (AF) is a public health concern because it is a major risk factor for stroke, heart failure, and death.[1,2] However, AF is often asymptomatic and paroxysmal, so stroke is often the first manifestation of AF.[3] Therefore, early AF detection and timely treatment initiation are necessary. Some countries actively recommend systematic screening for AF in elderly patients and patients who are at a high stroke risk,[3,4] but because the prevalence of AF is increasing, and is estimated to double in the next few decades, the need for reliable AF screening tools is urgent.[5,6]

The gold standard for definitive diagnosis of AF is a physician's diagnosis based on ECG recordings such as 12-lead ECG or Holter ECG. The detection rate of AF could be improved if these tests were performed randomly on patients who visit a medical institution, but the benefits of such an approach have not been proven to outweigh the increased medical staff labor and medical costs.[7] In clinical practice, additional ECG recordings are generally performed when deemed necessary by the physician, but it is not easy for a non-cardiologist to actively suspect AF based on pulse check or auscultatory techniques alone, which may lead to misdiagnosis.[8] Recently, AF detection using wearable devices has shown promise,[9–11] but given the current high prevalence of AF among the elderly, and the high proportion of asymptomatic patients, it remains to be seen how widespread the use of these relatively expensive devices, which require a certain degree of proficiency in operation, will be among elderly patients as a screening tool for arrhythmia.

The strongest risk factor for AF is hypertension, with an estimated prevalence of approximately 30–50% of the global population,[12–14] and timely intervention for hypertension plays an important role in reducing new-onset AF, as well in reducing the risk of complications, such as intracranial bleeding and stroke after anticoagulation therapy.[15,16] In other words, blood pressure (BP) monitoring is

Received February 7, 2024; accepted February 8, 2024; J-STAGE Advance Publication released online March 22, 2024 Time for primary review: 1 day
Department of Cardiorenal and Cerebrovascular Medicine, Faculty of Medicine, Kagawa University, Kagawa, Japan
Mailing address: Makoto Ishizawa, MD, PhD, Department of Cardiorenal and Cerebrovascular Medicine, Faculty of Medicine, Kagawa University, 1750-1 Ikenobe, Miki, Kita-gun, Kagawa 761-0793, Japan. email: ishizawa.makoto@kagawa-u.ac.jp

ISSN-2434-0790

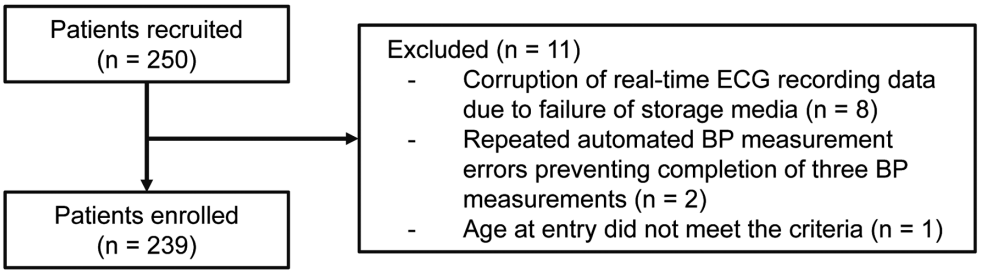

Figure. Flowchart of patient recruitment and participation. BP, blood pressure.

essential for AF management. Automated BP monitors are single devices that have the potential to simultaneously monitor BP and screen for AF. They can obtain pulse wave information through the cuff pressure sensor, making it possible to detect fluctuations in the pulse wave interval during BP measurement. There have been reports on the use of the Microlife and Omron automated BP monitors to detect AF during BP measurement. The sensitivity and specificity of these BP monitors for AF diagnosis are reported to be 81–100% and 89–99%, respectively, with varying results depending on the prevalence of AF and whether patients with arrhythmias besides AF are included in the study or not.[17–20]

Recently, Kabutoya et al proposed a specialized algorithm for AF detection based on the irregular heartbeat (IHB) detector built into A&D automated BP monitors.[21] Watanabe et al conducted a clinical study of patients in sinus rhythm and patients with AF, and reported that the new IHB algorithm equipped with the A&D automated BP monitor was extremely accurate for AF diagnosis, with a sensitivity of 99% and a specificity of 99%.[22] However, that clinical study did not include patients with arrhythmias other than AF, so its usefulness in the real-world clinical setting in which various types of arrhythmia are observed is still uncertain.

The primary objective of this study was to evaluate the performance of the IHB algorithm with the A&D automated BP monitor for AF diagnosis in clinical practice by conducting a clinical study on consecutive patients with and without AF and other arrhythmias. In addition, the secondary objective was to analyze the usefulness of the IHB algorithm in clinical practice by comparing its performance with that of automated ECG analysis software for AF diagnosis.

Methods

Study Design and Patients

We designed a single-center, prospective, observational study. It was approved by the Ethics Committee of Kagawa University Faculty of Medicine (ethics approval no. 2020-001), and conducted in accordance with the ethical standards of the responsible committee on human experimentation and with the 1964 Declaration of Helsinki and its later amendments. We recruited 250 patients aged ≥20 years without pacemakers or implantable cardioverter defibrillators who visited outpatient clinics or who were hospitalized at Kagawa University Hospital between September 2020 and December 2021. Patients who were unable to undergo BP measurements with a cuff around the upper arm in the seated position were excluded from the study. All patients provided written informed consent. Of the 250 patients, 11 were excluded from the analysis for the following reasons: age <20 years after informed consent and measurement (n=1), lack of real-time ECG data due to recording media malfunction (n=8), measurement interruption at the discretion of the attending physician due to patient complaints of distress over repeated cuff inflation (n=1), and exceeded the prescribed number of BP measurements due to repeated automatic BP measurement errors (n=1). Finally, the data from 239 patients were analyzed (**Figure**).

Procedure

The automated BP monitor UM-212 (A&D Co., Ltd., Tokyo, Japan), which is intended for clinical use at home and at healthcare facilities, incorporates the proprietary IHB algorithm for AF detection. IHB was defined when the proportion of pulse waves that varied by >15% from the mean of the pulse peak interval was >20% of the total pulse wave count.[21,22]

For each patient, BP was measured 3 times after a 5-min rest in the seated position. Between measurements, the patient was allowed to rest for ≥60 s. After the cuff was inflated above systolic pressure, the cuff pressure was reduced gradually. If BP measurement error occurred, an additional BP measurement was taken only once. The pulse wave intervals obtained during the cuff deflation phase were automatically analyzed by the proprietary IHB algorithm in the device. Systolic BP, diastolic BP, pulse rate, and number of IHBs were recorded.

Real-time 3-lead ECG (ESP-350, Fukuda Denshi Co. Ltd., Tokyo, Japan) was recorded continuously for ≥30 s from the start to the end of each BP measurement. The diagnostic results obtained from the built-in automatic ECG analysis software were shown on the display after each ECG recording. Independent of the diagnostic results of the ECG analysis software, 2 cardiologists interpreted the ECG and made the final diagnosis. If arrhythmias other than AF, such as extrasystoles, were confirmed at the final ECG diagnosis, they were classified as non-AF arrhythmias, even if the basic rhythm was sinus rhythm. The patients with sinus arrhythmia were classified as having sinus rhythm because sinus arrhythmia is judged as being clinically harmless.

The diagnostic performance of the IHB algorithm and the ECG analysis software for AF was evaluated accord-

Table 1. Patients' Baseline Characteristics

	All (n=239)	AF (n=31)	Non-AF (n=208)	P value*
Age (years)	67.8±12.7	70.4±11.8	67.2±12.8	0.027
Male (%)	62.3	67.8	61.5	0.557
Body mass index (kg/m^2)	23.8±3.9	24.6±3.3	23.6±3.9	0.076
Systolic BP (mmHg)	131.3±21.2	122.9±22.9	132.5±20.7	0.027
Diastolic BP (mmHg)	79.1±12.4	79.5±14.5	78.9±12.7	0.545
Pulse rate (beats/min)	68.0±13.1	74.7±15.2	67.1±12.5	0.017
Comorbidities (%)				
Hypertension	63.9	48.4	63.9	0.114
Congestive heart failure	31.3	41.9	29.3	0.097
Ischemic heart disease	20.9	16.1	21.6	0.637
Diabetes mellitus	22.1	22.6	22.1	1.000
TIA/cerebral infarction	6.7	6.5	6.7	1.000
Medications (%)				
Antithrombotic drug	65.6	100	60.6	<0.001
Antiarrhythmic drug	31.7	38.7	30.8	0.411
β-blocker	53.1	71.0	50.5	0.035
Ca channel blocker	41.8	38.7	42.3	0.846
ACE-I/ARB	57.7	58.1	57.7	1.000
MRA/ARNI	9.6	12.9	9.1	0.514
Diuretic	24.3	54.8	19.7	<0.001

Data are expressed as the mean±standard deviation. *P values were calculated using Student's t-test for continuous variables and Fisher's exact test for categorical variables in comparing the characteristics of patients with AF and with non-AF. AF, atrial fibrillation; ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; MRA, mineralocorticoid receptor antagonist; TIA, transient ischemic attack.

ing to sensitivity, specificity, and accuracy calculated from a 2×2 contingency table using the final ECG diagnosis of the 2 cardiologists as the reference standard. The evaluations were performed for each per-measurement unit and per-patient unit. For the per-patient evaluation, the sensitivity, specificity, and accuracy of the IHB algorithm and the ECG analysis software for AF diagnosis were calculated for combinations of 2 measurements (first and second) and 3 measurements (first, second, and third), respectively, to determine the effect of multiple measurements per patient on diagnostic performance.

Statistical Analysis

The baseline characteristics of the patients are expressed as the mean±standard deviation. Student's t-test for continuous variables and Fisher's exact test for categorical variables were used to compare the characteristics of the AF and non-AF patients. In the 2×2 contingency table, Fisher's exact test was performed to evaluate the statistical association between the results of the IHB algorithm or the ECG analysis software and the final AF diagnosis, which was judged significant at $P<0.05$. The 95% confidence intervals for sensitivity, specificity, and accuracy were calculated using the Agresti–Coull method. The degree of agreement between the diagnostic results of the IHB algorithm or the ECG analysis software and the final diagnostic results for each condition was evaluated by calculating the kappa coefficient, with a value of ≥0.61 representing substantial agreement and a value of ≥0.81 representing almost perfect agreement. All calculations were performed with JMP Pro software, version 15.0 (SAS Institute, Cary, NC, US).

Results

The baseline characteristics of the patients are shown in **Table 1**. According to the ECG interpretations by the 2 cardiologists, 31 patients (13%) were diagnosed with AF, either persistent or permanent AF, with a heart rate controlled with oral medication, and stable symptoms. Of the remaining 208 non-AF patients (87%), 135 patients (56%) were in sinus rhythm and 73 patients (31%) had non-AF arrhythmias. The 73 patients with non-AF arrhythmias included 30 patients with premature atrial contractions (PACs), 31 patients with premature ventricular contractions (PVCs), 4 patients with both PACs and PVCs, 4 patients with a short run of PACs, 3 patients with PACs with block, and 1 patient with atrial tachycardia. The mean age of the patients was 67.8±12.7 years; 164 patients (69%) were ≥65 years of age, 78 patients (33%) were ≥75 years of age, and 1 patient (0.4%) was ≥90 years of age. Patients with AF were older, had a lower systolic BP, and a higher pulse rate than patients with non-AF. Regarding comorbidities under treatment based on medical record information, patients with AF had a lower incidence of hypertension and a higher incidence of heart failure compared with patients with non-AF. Contrary to the fact that hypertension plays a major role in the new onset of AF, the lower systolic BP and lower rate of treatment of hypertension in patients with AF in this study may be partly due to the chronicity of AF and the higher rate of β-blocker and diuretic use.

The diagnostic performance of the IHB algorithm and the ECG analysis software for AF diagnosis was evaluated for the first measurement only, second measurement only,

Table 2. 2×2 Contingency Table and Diagnostic Performance Values for the IHB Algorithm in the Per-Measurement Evaluation

	Final diagnosis		Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	Kappa
	AF	Non-AF				
IHB detection in 1st BP measurement						
Positive	30	21	96.8% (82.4–100)	89.9% (85.0–93.4)	90.8% (86.4–93.9)	0.68
Negative	1	187				
IHB detection in 2nd BP measurement						
Positive	31	17	100% (86.9–100)	91.8% (87.2–94.9)	92.3% (88.8–95.6)	0.75
Negative	0	191				
IHB detection in 3rd BP measurement						
Positive	31	17	100% (86.9–100)	91.9% (87.2–94.9)	92.3% (88.8–95.6)	0.75
Negative	0	191				
IHB detection per BP measurement (aggregation of all measurements)						
Positive	92	55	98.9% (93.6–100)	91.2% (88.7–93.2)	92.2% (90.0–93.9)	0.72
Negative	1	569				

AF, atrial fibrillation; BP, blood pressure; CI, confidence interval; IHB, irregular heartbeat.

Table 3. 2×2 Contingency Table and Diagnostic Performance Values for the ECG Analysis Software in the Per-Measurement Evaluation

	Final diagnosis		Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	Kappa
	AF	Non-AF				
AF diagnosis by ECG analysis software in 1st ECG recording						
Positive	27	7	87.1% (70.5–95.5)	96.6% (93.1–98.5)	95.4% (91.9–97.5)	0.80
Negative	4	201				
AF diagnosis by ECG analysis software in 2nd ECG recording						
Positive	28	3	90.3% (74.3–97.4)	98.6% (95.6–99.7)	97.5% (94.5–99.0)	0.89
Negative	3	205				
AF diagnosis by ECG analysis software in 3rd ECG recording						
Positive	29	5	93.5% (78.3–99.2)	97.6% (94.3–99.1)	97.1% (94.0–98.7)	0.88
Negative	2	203				
AF diagnosis by ECG analysis software per ECG recording (aggregation of all ECG recordings)						
Positive	85	13	91.4% (83.7–95.8)	97.9% (96.4–98.8)	97.1% (95.5–98.1)	0.87
Negative	8	611				

AF, atrial fibrillation; CI, confidence interval; ECG, electrocardiogram.

third measurement only, and all measurements, respectively (**Tables 2**,**3**). For the IHB algorithm, the first measurement had a sensitivity of 96.8% due to 1 false-negative result, and the second and third measurements had a sensitivity of 100% (no false-negative results). The IHB algorithm showed a certain number of false-positive results for each of the 3 measurements, with a specificity of approximately 90%. In the aggregation of all 717 measurements, the IHB algorithm yielded only 1 false-negative result, but 55 false-positive results were detected, all of them in patients with non-AF arrhythmias. The sensitivity, specificity, and accuracy of the IHB algorithm for AF diagnosis were 98.9%, 91.2%, and 92.2%, respectively. For the ECG analysis software, there were few false-positive results in all 3 measurements, with specificity ranging from 96.6% to 98.6%. The ECG analysis software showed a certain number of false-negative results for each of the 3 measurements, with a sensitivity ranging from 87.1% to 93.5%. In the aggregation of all measurements, the ECG analysis software produced 8 false-negative results and 13 false-positive results out of 717 measurements. Of the 13 false-positive results, 6 were seen in patients with sinus rhythm, which differed from the IHB algorithm, where none of the false-positive results occurred in patients in sinus rhythm. The sensitivity, specificity, and accuracy of the ECG analysis software for AF diagnosis were 91.4%, 97.9%, and 97.1%, respectively.

We next evaluated the diagnostic performance of the IHB algorithm and the ECG analysis software for AF diagnosis in 239 patient units and by the number of BP measurements (**Tables 4**,**5**). When IHBs were detected in both the first and second BP measurements, the sensitivity, specificity, and accuracy for AF diagnosis were 96.8%, 94.2%, and 94.6%, respectively. When IHBs were detected in all 3 BP measurements, the sensitivity, specificity, and accuracy for AF diagnosis were 96.8%, 95.7%, and 95.8%, respectively. In the evaluation of the 3 measurements, false-positive results with the IHB algorithm were found in 9 of the 208 patients with non-AF, all of whom had non-AF arrhythmias (5 patients with PACs, 4 patients with PVCs), and false-negative results with the IHB algorithm were found in only 1 of 31 patients with AF. Similarly, when the ECG analysis software diagnosed AF in both the first and second measurements, the sensitivity, specificity, and accuracy for AF diagnosis were 77.4%, 99.5%, and

Table 4. 2×2 Contingency Table and Diagnostic Performance Values for the IHB Algorithm in the Per-Patient Evaluation

	Final diagnosis		Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	Kappa
	AF	Non-AF				
IHB detection in 1st BP measurement						
Positive	30	21	96.8% (82.4–100)	89.9% (85.0–93.4)	90.8% (86.4–93.9)	0.68
Negative	1	187				
IHB detection in both 1st and 2nd BP measurements						
Positive	30	12	96.8% (82.4–100)	94.2% (90.1–96.8)	94.6% (90.8–96.9)	0.79
Negative	1	196				
IHB detections in all 3 BP measurements						
Positive	30	9	96.8% (82.4–100)	95.7% (91.9–97.8)	95.8% (92.4–97.8)	0.83
Negative	1	199				

AF, atrial fibrillation; BP, blood pressure; CI, confidence interval; IHB, irregular heartbeat.

Table 5. 2×2 Contingency Table and Diagnostic Performance Values for the ECG Analysis Software in the Per-Patient Evaluation

	Final diagnosis		Sensitivity (95% CI)	Specificity (95% CI)	Accuracy (95% CI)	Kappa
	AF	Non-AF				
AF decision in 1st ECG recording						
Positive	27	7	87.1% (70.5–95.5)	96.6% (93.1–98.5)	95.4% (91.9–97.5)	0.80
Negative	4	201				
AF decisions in both 1st and 2nd ECG recording						
Positive	24	1	77.4% (60.0–88.9)	99.5% (97.0–100)	96.7% (93.4–98.4)	0.84
Negative	7	207				
AF decisions in all 3 ECG recordings						
Positive	24	1	77.4% (60.0–88.9)	99.5% (97.0–100)	96.7% (93.4–98.4)	0.84
Negative	7	207				

AF, atrial fibrillation; CI, confidence interval; ECG, electrocardiogram.

96.7%, respectively. When the ECG analysis software diagnosed AF in all 3 measurements, the sensitivity, specificity, and accuracy for AF diagnosis were the same as when AF was diagnosed in the first two measurements. In the evaluation of 2 and 3 measurements, false-positive results with the ECG analysis software were found in only 1 of 208 non-AF patients, but that patient was in sinus rhythm (sinus arrhythmia), and false-negative results with the ECG analysis software were found in 7 of 31 patients with AF.

The frequency with which the ECG analysis software resulted in inconclusive arrhythmia was only 3 of 717 measurements (0.42%): 1 in a patient with PACs with block and 2 in patients with sinus arrhythmia. No inconclusive results were obtained from patients with AF.

Fisher's exact test was performed on all 2×2 contingency tables, and the results were all $P<0.01$, indicating a significant statistical association between the 2 variables. The kappa coefficient of the IHB algorithm corresponded to substantial agreement with the final diagnosis of AF in all conditions. The kappa coefficients of the ECG analysis software corresponded to almost perfect agreement, except for the evaluation of only the first measurement. With 3 measurements per patient, the kappa coefficient of the IHB algorithm was 0.83, equivalent to almost perfect agreement and comparable to the ECG analysis software.

Discussion

In this study, we clarified the performance of an IHB algorithm built into an A&D automated BP monitor for AF diagnosis in a real-world clinical setting under single and multiple measurement conditions. We also compared the diagnostic performance of the IHB algorithm for AF with that of ECG analysis software.

Implications of AF Detection Using Automated BP Monitors

In recent years, various efforts have been made to detect AF in the early stage, and the usefulness of wearable devices has become more widely recognized through multiple large-scale clinical trials.[10–14] The greatest advantage of wearable devices is that they may detect even paroxysmal AF, which lasts for a few minutes or less. However, it is not clear whether therapeutic intervention for patients with such very brief attacks will improve their prognosis.[23] Opportunistic screening, such as the use of automated BP monitors, may be difficult to detect AF that lasts only a very short time and is extremely infrequent, but conversely, AF detected by opportunistic screening is assumed to be at higher risk for complications and to require more treatment. The ASSERT trial has shown that among subclinical AF with a duration of 6 min or longer, the incidence of stroke is significantly higher with a duration of 24 h or longer.[24] Simply, continued daily BP measurements could detect AF that persists for more than 24 h. It has been noted that there is a trade-off between the opportunity to detect AF and the clinical severity of detected AF, and therefore, opportunistic screening for AF is not considered futile.[25] AF detection with automated BP monitors that are already

in clinical use is based on the detection of pressure pulse waves showing greater variability than the average pulse wave peak interval, and the IHB algorithm with the A&D UM-212 BP monitor is no exception.[17,20–22] Although such algorithms are technically simple and can be easily incorporated into mass-produced automated BP monitors, there is a risk of false-positive results if pulse waves that vary significantly from the mean peak interval occur frequently, such as in frequent extrasystolic arrhythmias. This is a common challenge for AF detection using automated BP monitors. Although it is theoretically impossible to completely eliminate the risk of false-positive results, each automated BP monitor manufacturer has developed its own algorithm to overcome this challenge. Previous clinical studies using automated BP monitors manufactured by Microlife and Omron have reported a sensitivity of 81–100% and a specificity of 90–95% for AF diagnosis, despite differences in subject populations, number of measurements, and various other conditions.[17–20] The photoplethysmography that is used in many smartwatches is another method of pulse wave detection, and a previous review has reported a sensitivity of 81–100% and a specificity of 85–100% for AF diagnosis.[26] However, in that review, only 5 of the 20 studies had both sensitivity and specificity ≥95% for AF diagnosis. Although not directly comparable to the results of the present study, those results arguably support the validity of the clinical use of automated BP monitors equipped with an IHB algorithm for AF diagnosis.

Diagnostic Performance of the IHB Algorithm for AF

We have previously reported that the Omron BP monitor with a simple IHB detector, which detects pulse waves that vary >25% compared with the mean pulse wave interval, can be optimized for AF detection if certain conditions (IHB detection ≥2/3 BP measurements and a maximum IHB detection ≥2 beats) are met. The disadvantages are that 3 BP measurements are always required and the operator has to manually count the number of IHBs and consider whether the conditions were met. In contrast, the A&D IHB algorithm automatically calculates the degree of variability (>15%) and its frequency (>20%) compared with the mean pulse wave interval for each BP measurement.[20] In a previous study comprising only patients in sinus rhythm and patients with AF, the performance of the IHB algorithm in diagnosing AF was excellent, with sensitivity and specificity values of 99%.[22] The present study also showed consistently high sensitivity (96.8–100%), regardless of whether the assessment was per measurement or per patient, but the specificity was low (89.9–91.2%), especially for the per measurement assessment, because the population included patients with non-AF arrhythmias. Nevertheless, several previous reports have shown that a promising way to reduce the false-positive rate as much as possible is to increase the number of measurements per patient.[19,20] In the present study, as the number of measurements per patient increased, the specificity increased without a decrease in sensitivity. When the number of measurements was increased to 2 and both were positive for IHB, the specificity was >94%, and when the number of measurements was increased to 3 and all were positive for IHB, the specificity reached >95% and the agreement with the final diagnosis was high (kappa coefficient >0.81). These characteristics may allow for tailor-made operations, such as performing 2 measurements routinely and adding a third BP measurement or ECG test only when both measurements are positive. It is also noteworthy that of the patients who had false-positive results with the IHB algorithm, none were in sinus rhythm. Clinical evidence suggests that frequent PACs and PVCs are strong predictors of AF, stroke, and cardiovascular events; therefore, it would not be entirely useless to detect such frequent extrasystolic arrhythmias as false-positives.[27,28]

Diagnostic Performance of the ECG Analysis Software for AF

Interestingly, the performance of the ECG analysis software for AF diagnosis showed low sensitivity and high specificity, contrary to that of the IHB algorithm. In the present study, false-negative results produced by the ECG analysis software were more frequently observed in patients with unclear F-wave detection and relatively low RR interval variability, and these patients were mainly misidentified as having extrasystolic arrhythmias. One of the possible causes is that the ECG waveforms under analysis were 3-lead ECG waveforms rather than 12-lead ECG waveforms. However, a physician was present for all measurements, and the ECG waveforms were performed in an environment that minimized noise from electromyography and body motion, so the quality of the ECG waveforms was assured, at least compared with the 1-channel ECG measurements using wearable smart devices, which are becoming more popular. In fact, AF detection using smart devices in the real-world setting has an unanalyzable ECG waveform rate of 17–26%,[29] whereas in the present study, only 0.42% were labeled as inconclusive arrhythmia by the ECG analysis software. These results suggest that although ECG analysis software is useful for excluding the diagnosis of AF, relying on it alone may lead to AF being missed. The subanalysis of the SAFE trial highlighted similar problems to those in the present study, namely the low sensitivity of the ECG analysis software and the inaccuracy of ECG-based diagnosis by primary care providers.[30] To date, a physician's diagnosis based on ECG is mandatory even when AF is detected by screening tools such as wearable smart devices.[3] It should be noted that, especially in the primary care setting, healthcare providers who are unfamiliar with arrhythmia diagnosis often rely on the results of the ECG analysis software, and even with ECG-based diagnosis, there is a risk of missing AF.

Combined Use of the IHB Algorithm and ECG Analysis Software

In general, tests with high sensitivity are useful for diagnosis of exclusion. The results of this study suggest that patients in sinus rhythm or with infrequent extrasystolic arrhythmias can be excluded with a high probability, especially if the IHB algorithm is negative after multiple measurements. Conversely, repeated positive findings of the IHB algorithm with routine BP monitoring at home or in primary care settings may prompt the patient or healthcare provider to suspect AF, potentially paving the way for an additional ECG assessment or consultation with a cardiologist. In contrast, tests with high specificity, such as the ECG analysis software, are useful for definitive diagnosis. Conducting ECG screening by focusing on a population with a high AF prevalence is expected to further improve its diagnostic accuracy and is more cost-effective than performing ECG haphazardly in patient populations. A 2-stage operation of AF screening using an automated BP monitor equipped with the IHB algorithm as the first stage, and providing a definitive diagnostic aid for AF

using ECG analysis software for a population with high prevalence of AF as the second stage may be a promising method of efficient and reliable screening for AF even in primary care settings.

Study Limitations

First, 11 of the 250 enrolled patients were excluded from the analysis, and it cannot be denied that this may have had some influence on the performance evaluation. For the 8 patients excluded from the analysis because of lack of real-time ECG data due to recording malfunction, the BP and ECG measurements themselves were actually performed as prescribed. According to the physician's visual judgment at the time of measurement, 1 patient had AF and the IHB algorithm was positive for all 3 measurements, and 8 patients were in sinus rhythm and the IHB algorithm was negative for all 3 measurements. If we assume that the true ECG diagnosis was consistent with the visual judgment of the attending physician, the performance of the IHB algorithm may have been slightly underestimated. Second, the heart rate of patients with AF was higher than that of patients in sinus rhythm and patients with non-AF arrhythmias. As this observational study was conducted in daily practice, we were unable to make detailed evaluations of the effects of pulse rate. In addition, none of the patients presented with extreme bradycardia (<40 beats/min) or tachycardia (>120 beats/min). Therefore, the results of this study cannot be directly applied to patients with bradycardia and tachycardia. Third, patients who were unable to maintain a seated position were not included, and all measurements were performed in the presence of a physician. In other words, measurements were performed in an environment where artifacts, such as body movement, were unlikely to occur. In general practice or at home, artifacts may occur more frequently than in the study environment, reducing the diagnostic performance. Additionally, it is presumed that ECG analysis software is more susceptible to artifacts than automated BP monitors due to device characteristics. In addition, the diagnostic performance in bedridden patients, patients with tremors, and patients who are unable to follow instructions has not been validated. Finally, the patients in this study were enrolled via a cardiology outpatient clinic, so the prevalence of both AF and hypertension was likely to be higher than in the general population, potentially leading to selection bias. Further research is therefore needed to clarify the diagnostic performance of the IHB algorithm for AF detection in real-world clinical settings.

Conclusions

The IHB algorithm built into an A&D automated BP monitor demonstrated high diagnostic performance for AF in general cardiology patients, especially when multiple measurements were obtained. The high diagnostic sensitivity of the IHB algorithm for AF, which can be used clinically on its own, has the potential for more reliable AF screening when combined with ECG analysis software with high diagnostic specificity.

Acknowledgments

This work was supported by a joint research grant from A&D Co., Ltd. (Tokyo, Japan). We thank Mr. Atsufumi Sato, of A&D Co., Ltd., for his advice on the use of the A&D automated BP monitor. We appreciate the assistance of Terue Tanii and Tomoko Nakayama as clinical research coordinators. We thank Emily Woodhouse, PhD, from Edanz (https://jp.edanz.com/ac) for editing a draft of this manuscript.

Disclosures

This work was supported by a joint research grant from A&D Co., Ltd. (Tokyo, Japan).

IRB Information

This study was approved by the Ethics Committee of Kagawa University Faculty of Medicine (ethics approval no. 2020-001).

Data Availability

The deidentified participant data will not be shared.

References

1. Hayden DT, Hannon N, Callaly E, Chroinin DN, Horgan G, Kyne L. Rates and determinants of 5-year outcomes after atrial fibrillation-related stroke: A population study. *Stroke* 2015; **46:** 3488–3493.
2. Wang TJ, Larson MG, Levy D, Vasan RS, Leip EP, Wolf PA, et al. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: The Framingham Heart Study. *Circulation* 2003; **107:** 2920–2925.
3. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021; **42:** 373–498.
4. Chan NY, Orchard J, Agbayani MJ, Boddington D, Chao TF, Johar S, et al. Asia Pacific Heart Rhythm Society (APHRS) practice guidance on atrial fibrillation screening. *J Arrhythm* 2022; **38:** 31–49.
5. Krijthe BP, Kunst A, Benjamin EJ, Lip GY, Franco OH, Hofman A, et al. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. *Eur Heart J* 2013; **34:** 2746–2751.
6. Hermans ANL, Gawalko M, Dohmen L, van der Velden RMJ, Betz K, Duncker D, et al. Mobile health solutions for atrial fibrillation detection and management: A systematic review. *Clin Res Cardiol* 2022; **111:** 479–491.
7. Jonas DE, Kahwati LC, Yun JDY, Middleton JC, Coker-Schwimmer M, Asher GN. Screening for atrial fibrillation with electrocardiography: Evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2018; **320:** 485–498.
8. Fitzmaurice DA, Hobbs FD, Jowett S, Mant J, Murray ET, Holder R, et al. Screening versus routine practice in detection of atrial fibrillation in patients aged 65 or over: Cluster randomised controlled trial. *BMJ* 2007; **335:** 383.
9. Perez MV, Mahaffey KW, Hedlin H, Rumsfeld JS, Garcia A, Ferris T, et al. Large-scale assessment of a smartwatch to identify atrial fibrillation. *N Engl J Med* 2019; **381:** 1909–1917.
10. Guo Y, Wang H, Zhang H, Liu T, Liang Z, Xia Y, et al. Mobile photo-plethysmographic technology to detect atrial fibrillation. *J Am Coll Cardiol* 2019; **74:** 2365–2375.
11. Lubitz SA, Faranesh AZ, Selvaggi C, Atlas SJ, McManus DD, Singer DE, et al. Detection of atrial fibrillation in a large population using wearable devices: The Fitbit Heart Study. *Circulation* 2022; **146:** 1415–1424.
12. Huxley RR, Lopez FL, Folsom AR, Agarwal SK, Loehr LR, Soliman EZ, et al. Absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors: The Atherosclerosis Risk in Communities (ARIC) study. *Circulation* 2011; **123:** 1501–1508.
13. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, et al. Global disparities of hypertension prevalence and control: A systematic analysis of population-based studies from 90 countries. *Circulation* 2016; **134:** 441–450.
14. Verdecchia P, Angeli F, Reboldi G. Hypertension and atrial fibrillation doubts and certainties from basic and clinical studies. *Circ Res* 2018; **122:** 352–368.
15. Manolis AJ, Rosei EA, Coca A, Cifkova R, Erdine SE, Kjeldsen S, et al. Hypertension and atrial fibrillation: Diagnostic approach,

prevention and treatment: Position paper of the working group 'Hypertension Arrhythmias and Thrombosis' of the European Society of Hypertension. *J Hypertens* 2012; **30:** 239–252.
16. Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischemic stroke and bleeding in 182 678 patients with atrial fibrillation: The Swedish Atrial Fibrillation cohort study. *Eur Heart J* 2012; **33:** 1500–1510.
17. Wiesel J, Wiesel D, Suri R, Messineo FC. The use of a modified sphygmo-manometer to detect atrial fibrillation in outpatients. *Pacing Clin Electrophysiol* 2004; **27:** 639–643.
18. Kearley K, Selwood M, Van den Bruel A, Thompson M, Mant D, Hobbs FR, et al. Triage tests for identifying atrial fibrillation in primary care: A diagnostic accuracy study comparing single-lead ECG and modified BP monitors. *BMJ Open* 2014; **4:** e004565, doi:10.1136/bmjopen-2013-004565.
19. 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:** 1046–1048.
20. Ishizawa M, Noma T, Izumi T, Tani R, Inoue T, Nasu E, 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:** 2428–2433.
21. Kabutoya T, Imai Y, Hoshide S, Kario K. Diagnostic accuracy of a new algorithm to detect atrial fibrillation in a home blood pressure monitor. *J Clin Hypertens* 2017; **19:** 1143–1147.
22. Watanabe T, Tomitani N, Yasui N, Kabutoya T, Hoshide S, Kario K. Assessment of a new algorithm to detect atrial fibrillation in home blood pressure monitoring device among healthy adults and patients with atrial fibrillation. *J Clin Hypertens* 2021; **23:** 1085–1088.
23. Svendsen JH, Diederichsen SZ, Højberg S, Krieger DW, Graff C, Kronborg C, et al. Implantable loop recorder detection of atrial fibrillation to prevent stroke (The LOOP Study): A randomised controlled trial. *Lancet* 2021; **398:** 1507–1516.
24. Van Gelder IC, Healey JS, Crijns HJGM, Wang J, Hohnloser SH, Gold MR, et al. Duration of device-detected subclinical atrial fibrillation and occurrence of stroke in ASSERT. *Eur Heart J* 2017; **38:** 1339–1344.
25. Brandes A, Stavrakis S, Freedman B, Antoniou S, Boriani G, Camm AJ, et al. Consumer-led screening for atrial fibrillation: Frontier Review of the AF-SCREEN International Collaboration. *Circulation* 2022; **146:** 1461–1474.
26. Gill S, Bunting KV, Sartini C, Cardoso VR, Ghoreishi N, Uh HW, et al. Smartphone detection of atrial fibrillation using photoplethysmography: A systematic review and meta-analysis. *Heart* 2022; **108:** 1600–1607.
27. Agarwal SK, Heiss G, Rautaharju PM, Shahar E, Massing MW, Simpson RJ Jr, et al. Premature ventricular complexes and the risk of incident stroke: The Atherosclerosis Risk In Communities (ARIC) Study. *Stroke* 2010; **41:** 588–593.
28. Gladstone DJ, Dorian P, Spring M, Panzov V, Mamdani M, Healey JS, et al. Atrial premature beats predict atrial fibrillation in cryptogenic stroke: Results from the EMBRACE Trial. *Stroke* 2015; **46:** 936–941.
29. Mannhart D, Lischer M, Knecht S, du Fay de Lavallaz J, Strebel I, Serban T, et al. Clinical validation of 5 direct-to-consumer wearable smart devices to detect atrial fibrillation: BASEL Wearable Study. *JACC Clin Electrophysiol* 2023; **9:** 232–242.
30. Mant J, Fitzmaurice DA, Hobbs FD, Jowett S, Murray ET, Holder R, et al. Accuracy of diagnosing atrial fibrillation on electrocardiogram by primary care practitioners and interpretative diagnostic software: Analysis of data from screening for atrial fibrillation in the elderly (SAFE) trial. *BMJ* 2007; **335:** 380.