Home Blood Pressure Can Predict the Risk for Stroke/Bleeding Events in Elderly Patients With Nonvalvular Atrial Fibrillation From the ANAFIE Registry

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BACKGROUND: Blood pressure (BP) fluctuates significantly in patients with atrial fibrillation (AF); office BP measurements seem insufficient to assess AF patient risk accurately. We hypothesized that home BP could better predict the risk of stroke/systemic embolic events (SEE) and major bleeding in patients with AF than office BP.

METHODS: In this prespecified subcohort study of the ANAFIE (All Nippon AF in the Elderly) Registry, we evaluated the impact of home BP on the risk of stroke/SEE, major bleeding, intracranial hemorrhage, all-cause death, and net cardiovascular outcome (a composite of stroke/SEE and major bleeding). At enrollment, home BP was measured twice in the morning and evening for 7 days.

RESULTS: In total, 4933 elderly patients (aged ≥75 years) with nonvalvular AF participated. Incidences of net cardiovascular outcome, stroke/SEE, major bleeding, and intracranial hemorrhage increased significantly with increasing home systolic BP (H-SBP). Compared with H-SBP <125 mm Hg, ≥145 mm Hg was associated with increased risk of these events. The association between H-SBP and the events was observed only in patients with ≥20 H-SBP measurements.

CONCLUSIONS: In elderly patients with nonvalvular AF, high H-SBP (≥145 mm Hg) was a significant predictor of stroke/SEE, major bleeding, and intracranial hemorrhage risk. Strict BP control guided by the increasing number of home BP measurements may provide an accurate clinical outcome risk assessment.

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Key Words: atrial fibrillation ■ blood pressure ■ elderly ■ embolism ■ hemorrhage

Atrial fibrillation (AF) is a major risk factor of ischemic stroke, affecting the life expectancy of elderly patients. The incidence and prevalence of AF increase with age. The ANAFIE (All Nippon AF in the Elderly) Registry, a prospective, observational study, was conducted to clarify the real-world clinical status and prognosis of ≥30,000 elderly patients aged ≥75 years with nonvalvular AF (NVAF).

Hypertension is an independent risk factor for stroke/systemic embolic events (SEE) and bleeding complications in patients with AF. Hypertension and AF can affect the same patient. Hypertension is thought to amplify the risk of
Hypertension is a modifiable component of the CHADS2, CHA2DS2-VASc, and HAS-BLED (hypertension, abnormal liver/renal function, stroke history, bleeding history or predisposition, labile prothrombin time international normalized ratio, elderly, drug/alcohol usage) scores. The BAT (Bleeding With Anti-thrombotic Therapy) Study showed that an increase in blood pressure (BP) is associated with a higher risk of intracranial hemorrhage (ICH), and guidelines recommend controlling office BP (O-BP) below 130 mm Hg.

Several factors should be considered when evaluating the effect of BP on the risk of cardiovascular events and prognosis in very elderly patients with AF. Systolic BP (SBP) and diastolic BP (DBP) fluctuate significantly in patients with AF compared with patients with sinus rhythm. The limited number of O-BP measurements performed in current clinical practice is insufficient for accurately assessing BP risk in patients with AF. The strength of the association between BP and cardiovascular disease risk is significantly different among age groups. In very elderly patients (75–89 years), the impact of elevated BP on cardiovascular disease risk becomes less obvious.

We hypothesized that home BP (H-BP) would be better at predicting the risk of stroke/systemic embolic events, major bleeding, and intracranial hemorrhage in elderly patients with nonvalvular atrial fibrillation (NVAF). In this prespecified H-BP subgroup study of the ANAFIE Registry, we evaluated the impact of H-BP on the risk of stroke/systemic embolic events, major bleeding, ICH, all-cause death, and net cardiovascular outcome (a composite of stroke/systemic embolic events and major bleeding).

**METHODS**

The authors declare that all supporting data are available within the article and its Supplementary Materials.

**Study Design**

The rationale and methodology of the ANAFIE Registry have been previously published. Ethical approvals were obtained from all relevant institutional review boards, the principal being the Ethics Committee of The Cardiovascular Institute (Tokyo, Japan). The trial was registered at University Hospital Medical Information Network (UMIN) Clinical Trials Registry. The study was conducted per the Declaration of Helsinki, local registry requirements, and ethical guidelines for clinical studies in Japan.

**Patients**

The main inclusion criteria were age ≥75 years at the time of informed consent, a definitive diagnosis of NVAF, and the ability to attend hospital visits. The only specific enrollment condition
for the H-BP subcohort study was that patients provided written consent to be enrolled and agreed to measure their H-BP using an oscillometric device with an arm cuff.15,16 The main exclusion criteria are listed in the Supplementary Methods. All participants gave informed consent for the main ANAFIE Registry and this subcohort study and were free to withdraw at any time.18

Study End Points
The study endpoints were net cardiovascular outcome (ie, composite of stroke/SEE and major bleeding), stroke/SEE, major bleeding, ICH, and all-cause death. These events that occurred during the follow-up period were recorded in duplicate. All endpoint events were adjudicated by cerebrovascular, cardiac, and bleeding event evaluation committees consisting of neurologists, cardiologists, and hematologists. Major bleeding was classified per the International Society on Thrombosis and Haemostasis definition (Supplementary Methods).17

Data Collection
The H-BP and O-BP measurement procedures were based on those described by Kario et al.16 After receiving guidance on correctly and accurately conducting H-BP readings, patients measured their H-BP four times/day, twice in the morning and twice in the evening, for 1 week within 60 days patients measured their H-BP four times/day, twice in the morning and twice in the evening, for 1 week within 60 days. These events that occurred during the follow-up period were recorded in duplicate. All endpoint events were adjudicated by cerebrovascular, cardiac, and bleeding event evaluation committees consisting of neurologists, cardiologists, and hematologists. Major bleeding was classified per the International Society on Thrombosis and Haemostasis definition (Supplementary Methods).17

Statistical Analysis
Detailed statistical analysis methods applied to the ANAFIE Registry data have been previously described.4,14 To clarify the impact of BP on stroke/SEE, major bleeding, ICH, all-cause death, and net cardiovascular outcome risk in this cohort, the Kaplan-Meier method was used to estimate event incidence and to illustrate event occurrence. BP categories were chosen per the JSH 2019 guidelines.18 A Cox proportional hazards model was used to calculate hazard ratios (HRs) and corresponding 95% CIs for event risk to evaluate the effect of BP. To evaluate the accuracy of home SBP (H-SBP) versus office SBP (O-SBP) in predicting event risk in patients with NVAF, given the tendency for patients with AF to experience fluctuations in BP, a likelihood ratio test was used to assess improvements in the goodness-of-fit model for each event of interest.19 The Akaike Information Criterion and Schwarz Bayesian Information Criterion were calculated. An additional analysis was performed using the SBP categories outlined in the American Heart Association 2017 guideline.20 P values for the incidence rate ratio (relative risk) were calculated using the Poisson regression model. A spline regression analysis was performed as described in Supplementary Methods. Statistical tests were 2-sided, and the significance level was defined as P<0.05. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Tokyo, Japan).

RESULTS

Patient Characteristics
From the total ANAFIE Registry population, 4933 patients participated in this subcohort study; 56.2% were men, and the average age was 81.4 years. The mean CHA2DS2-VASc and HAS-BLED scores were 4.4 and 1.8, respectively; 77.6% of patients had hypertension, and 93.0% used anticoagulants. The mean BP values were 127.8±13.1 mm Hg for H-SBP, 72.6±9.1 mm Hg for home DBP (H-DBP), 128.4±17.2 mm Hg for O-SBP, and 71.3±11.5 mm Hg for office DBP. The mean number of measurements was 24.7±6.2 for H-BP and 2 for O-BP. During the 2-year follow-up period, 115 stroke/SEE and 76 major bleeding events were reported (Table 1). Table S1 shows the main characteristics of patients enrolled in the overall ANAFIE Registry and this H-BP subcohort.

Systolic BP Analysis
H-SBP was categorized according to the JSH 2019 guidelines.18 The H-SBP category with the most patients was <125 mm Hg (n=2030 [41%]) followed by 125 to <135 mm Hg (n=1585 [32%]), 135 to <145 mm Hg (n=878 [18%]), and ≥145 mm Hg (n=440 [9%]).

In general, increases in these events were observed with increasing H-SBP and were significant for all outcomes except for stroke/SEE. All-cause death was lowest among patients in the 135 to <145 mm Hg group; the highest probability of occurrence was in the ≥145 mm Hg group (Figure 1).

Among patients in the <125 mm Hg group and the ≥145 mm Hg group, the respective incidence rates per 100 person-years were 1.67 and 3.24 (P<0.05) for net cardiovascular outcome, 1.03 and 2.10 for stroke/SEE (P<0.05), 0.74 and 2.10 for major bleeding (P<0.05), 0.55 and 1.73 for ICH (P<0.05), and 3.67 and 4.39 for all-cause death (P=0.337; Figure 2A).

Compared with H-SBP <125 mm Hg, H-SBP ≥145 mm Hg was significantly associated with higher incidences of net cardiovascular outcome (HR, 1.92 [95% CI, 1.21–3.06]; P=0.006), stroke/SEE (HR, 1.88 [95% CI, 1.05–3.37]; P=0.033), major bleeding (HR, 2.92 [95% CI, 1.58–5.42]; P=0.001), and ICH (HR, 3.07 [95% CI, 1.54–6.15]; P=0.002). There were no significant associations in other H-SBP categories (≥125 mm Hg to <135 mm Hg, ≥135 mm Hg to <145 mm Hg) for these outcomes. For all-cause death, H-SBP 135 to <145 mm Hg was significantly associated with a lower incidence compared with H-SBP <125 mm Hg (HR, 0.70 [95% CI, 0.49–1.00]; P=0.049; Figure 2B).

In patients with ≥20 H-SBP measurements, the incidence rates of net cardiovascular outcome, stroke/SEE, major bleeding, and ICH significantly increased in the H-SBP ≥145 mm Hg group compared with the <125...
Regarding O-SBP, none of the BP categories were significantly associated with increased risk of any events assessed (Figure S1). The goodness-of-fit of the models for predicting risks of the net cardiovascular outcome, major bleeding, and ICH were significantly improved by adding H-SBP, but not O-SBP, to the model, including mmHg group, but not all-cause death. Even in patients with <20 H-SBP measurements, the incidence rate of stroke/SEE was numerically higher at H-SBP ≥145 mmHg. There were no significant differences in clinical outcomes, including stroke/SEE, between the H-SBP ≥145 mmHg and <125 mmHg groups (Figure 3).

Table 1. Background Characteristics of Patients With No Events, Stroke/SEE, or Major Bleeding Events

| Characteristic               | Total; N=4933 | No events; n=4505 | Stroke/SEE; n=172 | Major bleeding; n=115 | Intracranial hemorrhage; n=57 | All-cause death; n=299 |
|-----------------------------|---------------|-------------------|-------------------|-----------------------|------------------------------|-----------------------|
| Age, y                      | 81.4±4.8      | 81.2±4.7          | 80.2±4.6          | 82.1±4.6              | 81.8±4.7                     | 81.5±4.7              |
| Men                         | 2770 (56.2)   | 2512 (55.8)       | 92 (53.5)         | 59 (51.3)             | 44 (57.9)                    | 34 (59.6)             |
| Body mass index, kg/m²      | 23.4±3.6      | 23.5±3.5          | 23.4±4.0          | 23.8±3.6              | 23.0±4.4                     | 23.3±3.7              |
| Creatinine clearance, mL/min| 49.1±17.1     | 49.9±16.9         | 47.8±17.4         | 48.6±17.6             | 47±18.0                      | 49±17.1              |
| <50 mL/min                  | 2180 (44.2)   | 1927 (42.8)       | 80 (45.6)         | 51 (44.3)             | 37 (48.7)                    | 25 (43.9)             |
| Comorbidities               | 4800 (97.3)   | 4381 (97.2)       | 167 (97.1)        | 113 (98.1)            | 73 (96.1)                    | 55 (96.5)             |
| Hypertension                | 3629 (77.6)   | 3495 (77.6)       | 138 (80.2)        | 94 (81.7)             | 60 (78.9)                    | 44 (77.2)             |
| Dyslipidemia                | 2132 (43.2)   | 1969 (43.7)       | 77 (44.8)         | 50 (43.5)             | 36 (47.4)                    | 27 (47.4)             |
| Diabetes                    | 1278 (25.9)   | 1155 (25.6)       | 62 (36.0)         | 44 (38.3)             | 25 (39.2)                    | 19 (33.3)             |
| Chronic kidney disease      | 926 (18.8)    | 819 (18.2)        | 28 (16.3)         | 20 (17.4)             | 14 (18.4)                    | 8 (14.0)              |
| Cardiac diseases            | 2725 (55.2)   | 2443 (54.2)       | 101 (57.8)        | 64 (55.7)             | 44 (59.7)                    | 25 (43.9)             |
| Atrial fibrillation type    | 2052 (41.6)   | 1914 (42.5)       | 58 (33.7)         | 37 (32.2)             | 33 (43.4)                    | 24 (42.1)             |
| Paroxysmal                  | 2052 (41.6)   | 1914 (42.5)       | 58 (33.7)         | 37 (32.2)             | 33 (43.4)                    | 24 (42.1)             |
| Nonparoxysmal               | 2881 (58.4)   | 2591 (57.5)       | 114 (66.3)        | 78 (67.8)             | 43 (56.6)                    | 33 (57.9)             |
| CHA2DS2-VASc score          | 4.4±1.3       | 4.4±1.3           | 4.8±1.4           | 5.0±1.4               | 4.5±1.4                      | 4.3±1.4              |
| HAS-BLED score              | 1.8±0.8       | 1.8±0.8           | 1.9±0.9           | 2.0±0.8               | 1.9±1.0                      | 2.0±0.9              |
| SBP, mm Hg                  | O-SBP*        | 128.4±17.2        | 128.8±16.9        | 128.3±18.9            | 128.7±16.5                   | 128.9±22.3            |
| H-SBP (morning/ evening, mean)†| 127.8±13.1   | 127.9±12.7        | 130.2±16.0        | 130.1±14.3            | 132.7±18.4                   | 131.8±16.5            |
| H-SBP (morning)‡            | 130.4±14.0    | 130.5±13.7        | 132.6±16.4        | 132.3±15.1            | 135.0±18.8                   | 134.0±17.0            |
| H-SBP (evening)§            | 125.1±13.7    | 125.1±13.4        | 128.0±16.9        | 127.2±15.2            | 131.0±19.2                   | 130.3±17.3            |
| DBP, mm Hg                  | O-DBP*        | 71.3±11.5         | 71.5±11.4         | 70.2±11.7             | 70.2±11.3                    | 69.7±12.2             |
| H-DBP (morning/ evening, mean)†| 74.5±9.7     | 74.6±9.6          | 75.9±11.0         | 75.8±10.5             | 75.4±11.4                    | 75.6±11.7             |
| H-DBP (morning)‡            | 70.6±9.4      | 70.7±9.3          | 72.0±10.6         | 71.8±9.8              | 72.4±11.5                    | 73.2±11.2             |
| Antithrombotics             | 3658 (72.1)   | 3355 (72.4)       | 125 (75.3)        | 85 (75.9)             | 56 (76.7)                    | 41 (73.2)             |
| Anticoagulants              | 4725 (95.0)   | 4190 (93.0)       | 166 (96.5)        | 111 (96.5)            | 74 (97.4)                    | 55 (96.5)             |
| Warfarin                    | 1092 (22.1)   | 979 (21.7)        | 48 (27.9)         | 31 (27.0)             | 21 (27.6)                    | 16 (28.1)             |
| DOAC                        | 3494 (70.8)   | 3207 (71.2)       | 118 (68.6)        | 80 (69.6)             | 53 (69.7)                    | 39 (68.4)             |
| Dabigatran                  | 357 (7.2)     | 334 (7.4)         | 9 (5.2)           | 7 (6.1)               | 2 (2.6)                      | 0                   |
| Rivaroxaban                 | 1184 (24.0)   | 1076 (23.9)       | 41 (23.8)         | 31 (27.0)             | 17 (22.4)                    | 14 (24.6)             |
| Apixaban                    | 1184 (24.0)   | 1096 (24.3)       | 46 (26.7)         | 29 (25.2)             | 22 (28.9)                    | 16 (28.1)             |
| Edoxaban                    | 769 (15.6)    | 701 (15.6)        | 22 (12.8)         | 13 (11.3)             | 12 (15.8)                    | 9 (15.8)              |

Data are n (%) or mean±SD. BP indicates blood pressure; CV, cardiovascular; DBP, diastolic blood pressure; DOAC, direct oral anticoagulant; HAS-BLED, hypertension, abnormal liver/renal function, stroke history, bleeding history or predisposition, labile prothrombin time international normalized ratio, elderly, drug/alcohol usage; H-DBP, home diastolic blood pressure; H-SBP, home systolic blood pressure; O-DBP, office diastolic blood pressure; O-SBP, office systolic blood pressure; SBP, systolic blood pressure; and SEE, systemic embolic events. *Mean value measured twice at entry (2 measurements). †Mean values measured twice in the morning and evening for 7 consecutive days at entry (24.7±6.2). ‡Mean measured twice in the morning for 7 consecutive days at entry (n=4924, 12.6±2.8). §Mean value measured twice in the evening for 7 consecutive days at entry (n=4763, number of measurements 12.6±2.8).
only confounders (Table 2). Similar results were shown by Akaike Information Criterion and Schwarz Bayesian Information Criterion (Table S2).

**Home Diastolic BP Analysis**

H-DBP was also categorized according to the JSH 2019 guidelines. The incidence rates of net cardiovascular outcome, stroke/SEE, major bleeding, ICH, and all-cause death tended to increase with increasing H-DBP. Significant differences were observed for all outcomes among patients with H-DBP ≥90 mm Hg compared with <75 mm Hg, except for all-cause death (Figure S2).

Cox multivariate regression analysis also showed that compared with H-DBP <75 mm Hg, H-DBP ≥90 mm Hg was significantly associated with higher incidences of net cardiovascular outcome (HR, 3.17 [95% CI, 1.82–5.52]; P<0.001), stroke/SEE (HR, 2.46 [95% CI, 1.16–5.20]; P=0.019), major bleeding (HR, 4.03 [95% CI, 1.85–8.76]; P<0.001), and ICH (HR, 4.79 [95% CI, 2.03–11.28]; P<0.001; Figure S3). H-DBP 75 to <85 mm Hg was significantly associated with a lower incidence for all-cause death (HR, 0.72 [95% CI, 0.54–0.95]; P=0.020).

**Additional Analysis**

Per the American Heart Association 2017 guideline, the incidence rates of net cardiovascular outcome, stroke/SEE, major bleeding, and ICH were significantly increased in the H-SBP ≥145 mm Hg group compared with the <130 mm Hg group (Figure S4).

In the spline regression analysis, the H-SBP value for minimum risks of net cardiovascular outcome and major bleeding was 118 mm Hg. The H-SBP values at which the lower limit of the 95% CI exceeded a relative risk of 1 were 143 and 142 mm Hg, respectively (Figure S5).

Table S3 shows the incidence rates by type of hypertension. Masked hypertension (defined as H-SBP ≥145 mm Hg/O-SBP <160 mm Hg) was associated with significantly higher incidence rates of net cardiovascular outcome, stroke/SEE, major bleeding, and ICH. Sustained hypertension (H-SBP ≥145 mm Hg/O-SBP ≥160 mm Hg) was associated with an increased risk of major bleeding. However, in the white coat hypertension (H-SBP <145 mm Hg/O-SBP ≥160 mm Hg) group, there was no increase in the incidence rates of clinical outcomes. As a result of setting the type of hypertension with different criteria of SBP, sustained hypertension (defined as H-SBP ≥135 mm Hg/O-SBP ≥160 mm Hg) was associated with significantly higher incidence rates of net cardiovascular outcome, major bleeding, and ICH (Table S4). Table S5 shows the causes of death reported in the subcohort study by H-SBP category.

**DISCUSSION**

This is the first large-scale real-world study of H-BP to show the importance of H-BP measurements in patients with NVAF. The incidence rates of net cardiovascular outcome, stroke/SEE, major bleeding, ICH, and all-cause death increased with increasing H-SBP, particularly H-SBP ≥145 mm Hg in elderly patients with NVAF. A significant association between high H-SBP and the
increased risk of clinical outcomes was observed only in patients with ≥20 H-SBP measurements. However, there was no correlation between the risk of any outcomes assessed in this study with O-SBP. Additionally, the goodness-of-fit analysis showed that adding H-SBP to the model significantly improved the risk prediction of net cardiovascular outcome, major bleeding, and ICH, but not O-SBP. Furthermore, this study showed that H-DBP ≥90 mm Hg was a significant risk factor for net cardiovascular outcome, stroke/SEE, major bleeding, and ICH.

In hypertensive patients, H-BP is a known risk factor for cardiovascular remodeling and cardiovascular events.12,13 Japanese and other guidelines recommend hypertension treatment using H-BP as a guide.
In HONEST (Home blood pressure measurement with Olmesartan Naive patients to Establish Standard Target blood pressure) and J-HOP (Japan Morning Surge-Home Blood Pressure), the total cardiovascular risk of hypertensive patients was predicted more strongly by H-BP than O-BP. Of note, the definitions of net outcome vary across studies. This study focused on major clinical events (stroke/SEE and bleeding) to determine the benefit of anticoagulant therapy and did not include all-cause death as a net cardiovascular outcome.

In AF, O-BP might not be an accurate BP assessment, given the high beat-to-beat BP variability. H-BP measurements may have the advantage of better reflecting actual BP, unaffected by phenomena such as the white coat effect. Furthermore, multiple measurements provide an average value that can overcome the BP variability in patients with AF and enable reliable risk assessment. Indeed, this analysis showed that ≥20 H-BP measurements significantly detected the risk of events such as major bleeding, ICH, and net cardiovascular outcomes in patients with H-SBP ≥145 mm Hg. When the number of H-BP measurements was low (<20 measurements), the predictive ability decreased (i.e., no significant association was observed between the incidence of events and BP measurements).
In our study, O-BP was not associated with stroke/SEE risk or other endpoints, possibly because of the masking effects of aging among the very elderly. The main analysis of ANAFIE Registry (N=32,275), reported an increased risk of stroke/SEE, but not major bleeding or all-cause death among patients with O-BP ≥140 mm Hg compared with <130 mm Hg (HR, 1.3; P=0.001). The difference in the effects of O-BP on the risk of stroke/SEE between the main analysis of ANAFIE Registry and this subcohort study is unclear because there were no obvious differences in the baseline patient characteristics (Table S1). There might have been a selection bias in this subcohort study as 4933 out of 32,275 patients gave informed consent after it was explained to them that they were required to take an H-BP measurement each day for 1 week, suggesting that patients with a high level of health literacy might have chosen to participate in this subcohort study.

The BAT study, including patients with cardiovascular and cerebrovascular diseases (with or without AF) found that increased SBP and DBP during the study increased the risk of developing ICH; the estimated BP cutoff to predict ICH was ≥130/81 mm Hg. The strength of the association between BP and cardiovascular disease risk is significantly different among age groups. In very elderly patients (75–89 years), the impact of elevated BP on cardiovascular disease risk becomes less obvious because the risks associated with aging itself mask the risks associated with increased BP. Further, because white coat hypertension increases in elderly patients, it becomes difficult to find a relationship between O-BP and cardiovascular risk. However, it should be noted that our study clarified the independent association between H-BP at ≥145 mm Hg and the increased risks of net cardiovascular outcome, stroke/SEE, major bleeding, and ICH, even in the elderly patients with NVAF aged ≥75 years, by analyzing a large number of H-BP measurements.

All-cause death is an important endpoint for elderly patients. The incidence rate of all-cause death among patients in the <125 mm Hg group and the ≥145 mm Hg group (3.67 and 4.39/100 person-years, respectively)
was high compared with other endpoints. A significant difference was observed between patients with H-SBP of <125 mm Hg versus 135 mm Hg to <145 mm Hg (incidence rate, 3.67 versus 2.35; HR, 0.70 [95% CI, 0.49—1.00]; P=0.049). The spline analysis of this event showed a J-curve pattern, which differed from other events. Regarding the cause of death, there was no remarkable difference in the incidence rate of cardiovascular death between H-SBP of <125 mm Hg versus 135 mm Hg to <145 mm Hg (incidence rate, 0.97 versus 0.78). Therefore, noncardiovascular death may contribute to the low incidence of all-cause death in the H-SBP 135 mm Hg to <145 mm Hg group. The findings from the current study differ from those of the SPRINT (Systolic Blood Pressure Intervention Trial) study.26 The SPRINT study reported that in patients with hypertension aged ≥75 years, treating SBP to a target of ≤120 mm Hg compared with a target of ≤140 mm Hg significantly reduced the incidence of all-cause death.26 Main reasons for this difference were that all patients in the current ANAFIE Registry had AF, whereas the SPRINT study enrolled patients with hypertension; the ANAFIE Registry is an observational study without BP targets, whereas the SPRINT study is a clinical trial in which patients were randomized by BP targets; and in the ANAFIE Registry, many patients associated with a high risk of death, such as frailty (36.2%) with low BP (125.5/68.9 mm Hg), were enrolled.27

The main study limitations have been reported; here, we list those specific to this subcohort study. Changes in H-BP during the follow-up period were not examined, and the follow-up period was relatively short; however, future studies using H-BP measurements within longer follow-up may be helpful for accurate risk assessment. O-BP was the average of two measurements obtained at one visit; a future study analyzing more O-BP readings may predict clinical outcomes risk in patients with NVAF. Patients did not use the same BP device for H-BP measurements; using a standard device may lead to less measurement bias. Selection bias was possible, but there was no significant difference in patient background in the present subcohort study versus the overall ANAFIE Registry population. The relative impact of a single risk factor decreases with advancing age; thus, these findings should be confirmed in a relatively younger patient population with NVAF. Only Japanese patients were included, but future studies should evaluate the relationship between H-BP and clinical outcomes in non-Japanese patients with NVAF aged ≥75 years.

PERSPECTIVES

For elderly patients with NVAF aged ≥75 years, more than 93% were on anticoagulant therapy in the ANAFIE Registry, H-SBP ≥145 mm Hg was significantly associated with an increase in the risk of net cardiovascular outcome, stroke/SEE, major bleeding, and ICH. O-SBP did not identify these increases in event risk. A significant association between H-SBP and clinical outcomes was observed only in patients with ≥20 H-SBP measurements. H-BP measurement was useful in identifying at-risk patients; therefore, strict BP control guided by an increased number of H-BP measurements should be recommended for elderly patients with NVAF.
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