

## Supplementary Online Content

Okumura K, Tomita H, Nakai M, et al. Risk factors associated with ischemic stroke in Japanese patients with nonvalvular atrial fibrillation. *JAMA Netw Open*. 2020;3(4):e202881. 10.1001/jamanetworkopen.2020.2881

**eTable 1.** Detailed Missing Data in the Study Patients

**eTable 2.** Patient Registration Period and Definition of Risk Factors in Each Registry

**eTable 3.** Competing Risk Regression Model Analysis

**eReferences.**

This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Detailed missing data in the study patients

	Number of missing data
Body mass index	1,824
Chronic heart failure	10
Hypertension	18
Diabetes	1
Type of atrial fibrillation	23
Creatinine	1,695
Hemoglobin	1,718
Event record during follow-up	81
Follow-up period	195
Oral anticoagulants	42

**eTable 2.** Patient registration period and definition of risk factors in each registry

Registry (reference)	J-RHYTHM Registry (1-3)	Fushimi AF Registry (4)	Shinken Database (5)	Keio interhospital Cardiovascular Studies (6)	Hokuriku-Plus AF Registry (7)
Patient registration	From January, 2009 to July, 2009	From February, 2011 ~ ongoing	From June, 2004 ~ ongoing	From January, 2012 to March, 2018	From May, 2013 to May, 2014
“C” Congestive heart failure	<ul style="list-style-type: none"> <li>Recent heart failure based on the criteria of CHADS<sub>2</sub> score</li> <li>Clinically diagnosed heart failure</li> </ul>	<ul style="list-style-type: none"> <li>History of hospitalization for heart failure</li> <li>Symptoms of heart failure (NYHA≥2)</li> <li>Left ventricular ejection fraction &lt;40%</li> </ul>	<ul style="list-style-type: none"> <li>Symptoms of heart failure (NYHA≥2)</li> </ul>	<ul style="list-style-type: none"> <li>History of hospitalization for heart failure</li> <li>Symptoms of heart failure</li> </ul>	<ul style="list-style-type: none"> <li>History of hospitalization for heart failure</li> <li>Symptoms of heart failure</li> <li>Treatment for heart failure</li> </ul>
“H” Hypertension	<ul style="list-style-type: none"> <li>Blood pressure ≥140/90 mmHg</li> <li>Antihypertensive drug</li> <li>History of hypertension</li> </ul>	<ul style="list-style-type: none"> <li>Blood pressure &gt;140/90 mmHg</li> <li>Antihypertensive drug</li> </ul>	<ul style="list-style-type: none"> <li>Blood pressure &gt;140/90 mmHg</li> <li>Antihypertensive drug</li> </ul>	<ul style="list-style-type: none"> <li>Blood pressure ≥140/90 mmHg</li> <li>Antihypertensive drug</li> <li>History of hypertension</li> </ul>	<ul style="list-style-type: none"> <li>Blood pressure &gt;140/90 mmHg</li> <li>Antihypertensive drug</li> </ul>
“D” Diabetes	<ul style="list-style-type: none"> <li>HbA1c ≥6.5%</li> <li>Treatment for diabetes</li> </ul>	<ul style="list-style-type: none"> <li>HbA1c &gt;6.5%</li> <li>Treatment for diabetes</li> </ul>	<ul style="list-style-type: none"> <li>HbA1c &gt;6.5%</li> <li>Treatment for diabetes</li> </ul>	<ul style="list-style-type: none"> <li>HbA1c &gt;6.5%</li> <li>Fasting plasma glucose &gt;126 mg/dL</li> <li>Random plasma glucose &gt;200 mg/dL</li> <li>Treatment for diabetes</li> </ul>	<ul style="list-style-type: none"> <li>HbA1c &gt;6.5%</li> <li>Fasting plasma glucose &gt;126 mg/dL</li> <li>Random plasma glucose &gt;200 mg/dL</li> <li>Treatment for diabetes</li> </ul>
“V” Vascular diseases	<ul style="list-style-type: none"> <li>Coronary artery disease</li> </ul>	<ul style="list-style-type: none"> <li>Myocardial infarction</li> <li>Peripheral artery disease</li> </ul>	<ul style="list-style-type: none"> <li>Myocardial infarction</li> <li>Peripheral artery disease</li> </ul>	<ul style="list-style-type: none"> <li>Coronary artery disease</li> <li>Peripheral artery disease</li> <li>Large vessel disease</li> </ul>	<ul style="list-style-type: none"> <li>Coronary artery disease</li> <li>Peripheral artery disease</li> <li>Large vessel disease</li> </ul>

NYHA indicates New York Heart Association Functional Classification, HbA1c; Hemoglobin A1c.

**eTable 3.** Competing risk regression model analysis

	Univariate		Multivariable		Stepwise	
	SHR (95%CI)	p-value	SHR (95%CI)	p-value	SHR (95%CI)	p-value
Age (<75 years)	Reference		Reference		Reference	
75-84 years	1.63 (1.26-2.11)	<0.001	1.60 (1.19-2.14)	0.002	1.74 (1.31-2.31)	<0.001
≥85 years	2.67 (1.89-3.78)	<0.001	2.04 (1.33-3.12)	0.001	2.41 (1.59-3.64)	<0.001
Female	1.36 (1.05-1.76)	0.02	1.20 (0.90-1.59)	0.22		
CHF	1.48 (1.14-1.93)	0.004	1.08 (0.81-1.44)	0.59		
Hypertension	1.63 (1.17-2.27)	0.004	1.51 (1.07-2.13)	0.02	1.60 (1.14-2.24)	0.007
Diabetes	1.21 (0.90-1.62)	0.21	1.09 (0.80-1.48)	0.58		
Previous stroke	3.08 (2.36-4.04)	<0.001	2.72 (2.04-3.62)	<0.001	2.75 (2.07-3.65)	<0.001
Vascular disease	1.34 (0.96-1.87)	0.09	1.03 (0.73-1.46)	0.86		
Type of AF (persistent/permanent)	1.61 (1.23-2.11)	<0.001	1.58 (1.18-2.11)	0.002	1.59 (1.21-2.10)	0.001
Low BMI <18.5 kg/m <sup>2</sup>	1.95 (1.33-2.86)	0.001	1.46 (0.98-2.19)	0.07	1.54 (1.04-2.29)	0.03
Creatinine ≥1.0 mg/dL	1.47 (1.13-1.90)	0.004	1.21 (0.92-1.60)	0.17		
Low hemoglobin	1.72 (1.33-2.24)	<0.001	1.18 (0.88-1.58)	0.28		
No oral anticoagulant	1.49 (1.14-1.95)	0.004	1.86 (1.38-2.51)	<0.001	1.86 (1.38-2.50)	<0.001

SHR indicates subhazard ratio, CI; confidence interval, CHF; congestive heart failure, AF; atrial fibrillation, BMI; body mass index.

## eReferences

1. Atarashi H, Inoue H, Okumura K, Yamashita T, Origasa H. Investigation of optimal anticoagulation strategy for stroke prevention in Japanese patients with atrial fibrillation-the J-RHYTHM Registry study design. *J Cardiol*. 2011;57(1):95-99.
2. Kodani E, Atarashi H, Inoue H, et al. Impact of blood pressure control on thromboembolism and major hemorrhage in patients with non-valvular atrial fibrillation: A subanalysis of the J-RHYTHM Registry. *J Am Heart Assoc*. 2016;5(9):e004075.
3. Okumura K, Inoue H, Atarashi H, Yamashita T, Tomita H, Origasa H. Validation of CHA<sub>2</sub>DS<sub>2</sub>-VASc and HAS-BLED scores in Japanese patients with nonvalvular atrial fibrillation: an analysis of the J-RHYTHM Registry. *Circ J*. 2014;78(7):1593-1599.
4. Akao M, Chun YH, Wada H, et al. Current status of clinical background of patients with atrial fibrillation in a community-based survey: the Fushimi AF Registry. *J Cardiol*. 2013;61(4):260-266.
5. Suzuki S, Otsuka T, Sagara K, et al. Nine-year trend of anticoagulation use, thromboembolic events, and major bleeding in patients with non-valvular atrial fibrillation- Shinken Database Analysis. *Circ J*. 2016;80(3):639-649.
6. Ikemura N, Kohsaka S, Kimura T, et al. Assessment of sex differences in the initial symptom burden, applied treatment strategy, and quality of life in Japanese patients with atrial fibrillation. *JAMA Netw Open*. 2019;2(3):e191145.
7. Hayashi K, Tsuda T, Nomura A, et al. Impact of B-type natriuretic peptide level on risk stratification of thromboembolism and death in patients with nonvalvular atrial fibrillation- The Hokuriku-Plus AF Registry. *Circ J*. 2018;82(5):1271-1278.