

Stroke, systemic embolism and bleeding rate in non-valvular atrial fibrillation patients without anticoagulation on the real world data in Japan

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Background: Anticoagulant therapy is recommended in patients with non-valvular atrial fibrillation (NVAF) for those with CHADS₂ ≥ 2 . However, there have been significant number of subjects with CHADS₂ ≥ 2 who receive no anticoagulation. Most of reported real world data have been collected mainly before wide spread use of DOAC. This study evaluated the clinical outcome of no anticoagulant drug therapy in NVAF.

Methods: This study is a non-interventional, observational, retrospective cohort study of NVAF patients in Mie-LIP Database, which is a regional clinical database joining 1 university hospital and 8 general hospitals in Mie prefecture in Japan. Patient enrolment was conducted from 1st Jan. 2016 to 31st Dec. 2018. The primary outcome events are ischemic stroke, systemic embolism, and bleeding events (bleeding to need a blood transfusion, intracranial bleeding, intraocular bleeding, and gastrointestinal bleeding).

Results: 7001 patients were included in the current analysis, 2550 patients, 36.4% were treated without any anticoagulant drug therapy. Table 1 shows patients with no anticoagulant drug therapy, mean age was 75.4

years and 42.2% of patients were female. The most frequent comorbidities included hypertension (50.0%), diabetes mellitus (28.2%), heart failure (14.0%), ischemic stroke (12.7%), vascular disease (14.4%) respectively. The annual incidence of ischemic stroke, systemic embolism per 100 person-years is 3.7, and that in each CHADS₂ group is 0: 1.4, 1: 1.4, 2: 3.2, 3–6: 8, respectively in Figure 1. The annual incidence of bleeding events is 1.5, and that in each CHADS₂ group is 0: 0.7, 1: 1.0, 2: 1.2, 3–6: 2.9, respectively.

Conclusions: Approximately one-thirds of subjects have not received any anticoagulation in the modern DOAC in daily clinical practice in Japan. The rate of ischemic stroke and systemic embolism increased by CHADS₂. Stroke or SEE rate was very low in subjects with CHADS₂ ≤ 1 , supporting no indication of anticoagulation in current guidelines. Regarding subjects with CHADS₂ ≥ 2 , considering the higher risk of stroke, use of anticoagulant drug therapy is recommended.

Table 1. Baseline patient characteristics

CHADS ₂ (n)	All (2550)	0 (460)	1 (712)	2 (692)	3–6 (686)
Age (years)	75.4±12.7	61.7±12.4	74.9±11.7	79.1±10.2	81.4±8.8
Male	1474 (57.8)	292 (63.5)	434 (61.0)	378 (54.6)	370 (53.9)
Female	1076 (42.2)	168 (36.5)	278 (39.0)	314 (45.4)	316 (46.1)
Weight (kg)	60.0±15.3	62.3±13.1	60.8±15.0	58.9±15.6	58.8±16.5
CrCL (mL/min)	59.0±30.3	76.4±49.6	60.7±23.0	54.2±21.3	50.7±21.7
Hypertension	1275 (50.0)	0	198 (27.8)	511 (73.8)	566 (82.5)
Diabetes	720 (28.2)	0	111 (15.6)	203 (29.3)	406 (59.2)
Heart failure	357 (14.0)	0	15 (2.1)	89 (12.9)	253 (36.9)
Stroke/TIA	325 (12.7)	0	0	32 (4.6)	293 (42.7)
Vascular disease	366 (14.4)	27 (5.9)	78 (11.0)	104 (15.0)	157 (22.9)
GI bleeding	25 (1.0)	4 (0.9)	7 (1.0)	5 (0.7)	9 (1.3)
Aspirin use	194 (7.6)	10 (2.2)	43 (6.0)	57 (8.2)	84 (12.2)
ADPReceptor use	145 (5.7)	9 (2.0)	39 (5.5)	34 (4.9)	63 (9.2)

Values are shown as mean \pm SD or n (%). TIA, transient ischemic attack; GI, gastrointestinal; ADPR, Adenosine diphosphate (ADP) receptor.

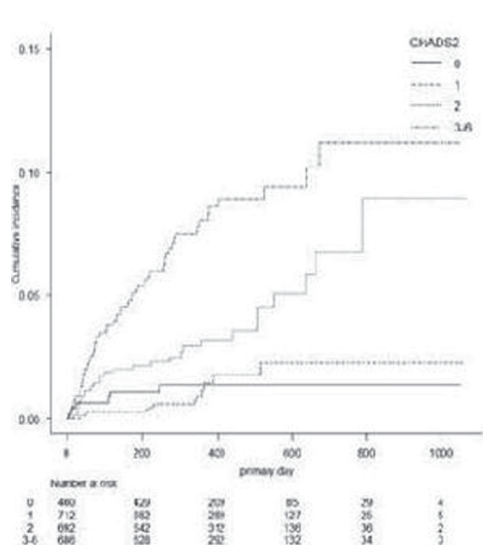


Figure 1. Kaplan-Meier curves for stroke or systemic embolism

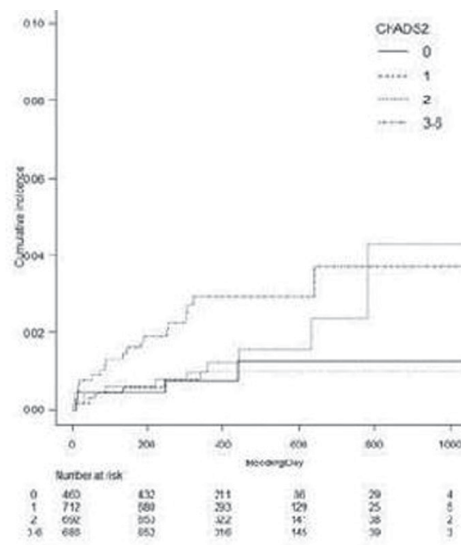


Figure 2. Kaplan-Meier curves for bleeding events