Current Status of Anticoagulation Therapy for Elderly Atrial Fibrillation Patients in Japan — From Hokuriku Atrial Fibrillation Trial —

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Background  The number of the elderly patients with atrial fibrillation (AF) is increasing, but the current status of anticoagulation therapy for elderly patients with AF in Japan is not clear.

Methods and Results  Among the patients registered in the “Hokuriku Atrial Fibrillation Trial (HAT) 1”, 365 AF patients aged ≥65 years were enrolled in this study. Warfarin was used for significantly less patients in the oldest group aged ≥85 years (36%) than in younger populations, but the percentage of antiplatelet use in this oldest population was largest (40%). The elderly group (≥85 years) was compared with a younger group aged between 75 and 84 years. Warfarin was given to 61% of the younger group compared with 36% in the elderly group. In the younger group, the more thromboembolic risks they had according to CHADS2 score, the more warfarin was used, whereas there was no clear trend in the usage of warfarin in the elderly group.

Conclusions  The number of elderly Japanese patients with AF taking warfarin is currently low, but because the population of elderly AF patients will increase in the future, there is a need for safe and suitable anticoagulation therapy for elderly patients.  

Key Words:  Aging; Anticoagulation; Atrial fibrillation; Japanese

Atrial fibrillation (AF) is associated with increasing morbidity and mortality, mainly because of thromboembolic complications. The incidence of AF in European patients aged >80 years was reported to be 9%, whereas in Japan, 1 report showed that 2.5% of subjects aged >80 years suffered permanent AF. Though the incidence of AF is quite low, the number of elderly patients with AF is increasing because of the aging of the Japanese population; aging is a known major thromboembolic risk factor for AF. Because anticoagulation therapy is reported to reduce the thromboembolic risk in nonvalvular AF by 68%, several guidelines recommend that AF patients aged >75 years should take anticoagulation therapy. Various reports have highlighted warfarin usage in Japan, but the current status of anticoagulation therapy for elderly Japanese AF patients (particularly those aged ≥85 years) is not clear. Thus, the purpose of this study was to describe current anticoagulation therapy protocols for elderly patients with AF in Japan.

Methods

Study Patients  This study was conducted from April 2005 to May 2008, involving 15 hospitals in the Hokuriku area, including 3 prefectures (Ishikawa, Toyama, and Fukui), and the 493 AF patients (307 males, 186 females; age range, 31–100 years) registered in the “Hokuriku Atrial Fibrillation Trial (HAT) 1: current situation survey of HAT”. The participating hospitals comprised 8 major hospitals (>200 beds), 5 small- and medium-sized hospitals (<200 beds) and 5 clinics.

Data Collection  Clinical data of the patients were registered on the Internet by the doctors in charge at each hospital and clinic. The following data were collected at the time of registration: sex, age, use of warfarin or antiplatelet agents, AF history, type of AF (paroxysmal, persistent or permanent), New York Heart Association (NYHA) functional class, history of cerebrovascular infarction or cerebral bleeding, and coexisting conditions including hypertension (HT), and diabetes mellitus (DM). Stroke risk scores were calculated according to the CHADS2 scheme (congestive heart failure (HF)=1 point, HT=1 point, age ≥75=1 point, DM=1 point, and prior stroke or transient ischemic attack=2 points).

Data Analysis  Baseline differences between age groups were evaluated with $\chi^2$ tests for categorical variables and Student’s t-test for continuous variables. Data are presented as mean±SD. Statistical significance was set at p<0.05.
Anticoagulation for Elderly Japanese AF Patients

Results

Of the 496 AF patients registered in the HAT1 study, 365 patients aged ≥65 years were enrolled in this study (mean age, 72±7 years); 289 cases from the major hospitals, 23 cases from the small- or medium-sized hospitals, and 53 cases from the clinics. The number of cases of paroxysmal, persistent, and permanent AF was 127 (35%), 38 (10%), and 200 (55%), respectively. The mean duration of AF was 19.0 years. The number of cases in each NYHA functional class was 277 (76%) in class I, 76 (21%) in class II, and 12 (3%) in class III. Associated diseases were HT in 242 cases (66%), cerebrovascular disease in 76 (21%), DM in 71 (19%), and ischemic heart disease (IHD) in 57 (16%). Fig 1 shows the distribution of the antithrombotic therapies according to the age of the patients. Patients taking both warfarin and antiplatelets were assigned to the warfarin group. None, patients not receiving antiplatelet or warfarin therapy.

Table 1 Baseline Characteristics and Warfarin Use by Age Group

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>75–84 years</th>
<th>p value</th>
<th>≥85 years</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (+)</td>
<td>(−)</td>
<td>All (+)</td>
<td>(−)</td>
</tr>
<tr>
<td>n</td>
<td>165</td>
<td>100</td>
<td>65</td>
<td>58</td>
</tr>
<tr>
<td>Male</td>
<td>90 (55)</td>
<td>58 (58)</td>
<td>32 (49)</td>
<td>NS</td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td>55 (33)</td>
<td>20 (20)</td>
<td>35 (54)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AF history (months)</td>
<td>87.3±88.9</td>
<td>104.9±97.9</td>
<td>60.2±65.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HT</td>
<td>116 (70)</td>
<td>71 (71)</td>
<td>45 (69)</td>
<td>NS</td>
</tr>
<tr>
<td>Heart failure</td>
<td>42 (25)</td>
<td>30 (30)</td>
<td>12 (18)</td>
<td>NS</td>
</tr>
<tr>
<td>DM</td>
<td>42 (25)</td>
<td>28 (28)</td>
<td>14 (22)</td>
<td>NS</td>
</tr>
<tr>
<td>CVA</td>
<td>40 (24)</td>
<td>32 (32)</td>
<td>8 (12)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cerebral bleeding</td>
<td>21 (13)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>NS</td>
</tr>
<tr>
<td>IHD</td>
<td>31 (19)</td>
<td>19 (19)</td>
<td>12 (18)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are mean ±SD or number (%).
*p<0.05 vs younger group.
AF, atrial fibrillation; HT, hypertension; DM, diabetes mellitus; CVA, cerebrovascular attack; IHD, ischemic heart disease.

Ethical Issues

The Ethical Committee of Kanazawa University Hospital granted permission for this study.

In order to know the characteristics of the very old patients (aged ≥85 years: elderly group), we compared them with patients aged between 75 and 84 years (younger group). Patient characteristics and warfarin use of the 2 study groups are shown in Table 1. There was no difference between the 2 study groups in sex, AF history, and percentage of paroxysmal AF, HT, IHD, or history of cerebral infarction or cerebral bleeding. The elderly group included more HF (p<0.05) and less DM (p<0.05) cases than the younger group. In the younger group, warfarin was used for more cases if AF was persistent or permanent (p<0.01), if patients had longer AF history (p<0.01), or if patients had a history of cerebrovascular attack (p<0.01). In the elderly group, there was no difference in the baseline characteristics between those who were taking or not taking warfarin. Among all registered subjects, only 2 cases had a history of cerebral bleeding: 1 in the younger group and 1 in the elderly group.

The distribution of antithrombotic treatment in the 2 groups according to CHADS2 risk score is shown in Fig 2. In the younger group, the percentage of warfarin use was 50% when their CHADS2 risk score was 1, and the ratio of warfarin use increased according to their thromboembolic risk; 100% of the patients took warfarin when the CHADS2 risk score was 6. On the other hand, in the elderly group...
Discussion

The current study reports the number of elderly Japanese AF patients taking warfarin in a real world setting. Among elderly Japanese AF patients aged ≥85 years, only 36% were on anticoagulation therapy, compared with 61% of patients in the 75–84-years group. In the younger group, the more thromboembolic risks they had, the more warfarin was used, whereas there was no clear trend in the usage of warfarin in elderly patients aged ≥85 years.

Despite the proven benefit of warfarin for preventing stroke in AF patients, its underutilization in Western countries has been reported, particularly among those aged >80 years (even hospitalized cohort patients) in whom warfarin usage was 45%. A previous Japanese report on nonvalvular AF showed that 48% of the patients aged >75 years were taking warfarin and, among patients who had no other risk factor than aging, only 22% had been given anticoagulation therapy. There are no detailed reports concerning elderly Japanese AF patients.

Our study showed that, among patients aged <85 years, 60% were on anticoagulation therapy, which was similar to other recent Japanese reports. Meanwhile, 36% of the patients aged ≥85 years were taking warfarin. Compared with Western reports, there are similarities in the usage of warfarin according to age.

In a previous Japanese report, the reasons for not using warfarin were discussed. The mean age of that study population was 66.6 years and although contraindication for warfarin was found in only 22.6% of the cases, the paradoxical nature of NVAF seemed to be the main reason for not using warfarin. In the present study, patients in the younger group with paroxysmal AF or a shorter history of AF took less anticoagulation therapy. Also, the tendency for taking warfarin according to the CHADS2 risk score was similar to that in a previous study in a younger group. In other words, the more thromboembolic risks accumulated, the more warfarin was used.

Far less usage of warfarin occurred for elderly Japanese patients aged ≥85 years in this study. No single characteristic or risk was related to the ratio of warfarin use in this group. Also, there was no relationship between the thromboembolic risk of the patient according to the CHADS2 risk score and the ratio of warfarin use in this population. On the other hand, antiplatelet agents were used for more patients in the elderly group. A recent study has shown that antiplatelet agents are inferior to warfarin for preventing not only embolism but also intracranial hemorrhage in elderly patients. In a prospective study for admitted AF patients in the United States, bleeding and falls were the main reason for not using warfarin in elderly patients aged ≥80 years. Though we have no data about systemic bleeding or falls in this study, it is possible that much older patients have additional constraints on taking anticoagulation therapy and so they are compelled to take antiplatelet agents in the clinical setting.

Conclusions

The number of elderly Japanese AF patients taking warfarin is currently low, but because the number of elderly AF patients will increase in the future, establishment of safe and suitable anticoagulation therapy for elderly patients is required.

Acknowledgment

We thank all the participants in the Hokuriku Atrial Fibrillation Trial, who are listed in Appendix 1.

References


**Appendix 1**

The following investigators participated in this study.

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