Patient Satisfaction with Direct Oral Anticoagulants and Warfarin
Findings from the SAKURA AF Registry
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Summary
The burden of anticoagulation treatment affects patient satisfaction, which in turn affects adherence to treatment. Thus, we must thoroughly understand the advantages of direct oral anticoagulants (DOACs) over vitamin K antagonists (VKAs)/warfarin given for stroke prevention in patients with atrial fibrillation (AF). We compared satisfaction with anticoagulation therapy between 654 DOAC and 821 warfarin users enrolled in the SAKURA AF Registry. Satisfaction was assessed by means of the Anti-Clot Treatment Scale (ACTS), which includes 12-item burdens and 3-item benefits scales, and the treatment satisfaction questionnaire for medication II (TSQM II), which includes 2-item effectivness, 3-item side effects, 3-item convenience, and 2-item global satisfaction domains. There were no significant between-group differences in TSQM II convenience (67.6 ± 14.5 versus 68.9 ± 14.5, P = 0.280), effectiveness (65.0 ± 13.3 versus 66.0 ± 15.0, P = 0.422), side effects (93.6 ± 13.7 versus 92.8 ± 14.4, P = 0.067), and global satisfaction (64.7 ± 14.9 versus 66.0 ± 14.6, P = 0.407) scores. In contrast, although there was no significant between-group difference in the ACTS benefits scores (9.8 ± 3.1 versus 10.1 ± 3.2, P = 0.051), the ACTS burdens scores (54.5 ± 6.3 versus 52.7 ± 6.9, P < 0.0001) were significantly higher in the DOAC users, independent of age, sex, and DOAC type. We can expect greater burden satisfaction with anticoagulation treatment in patients given a DOAC versus VKA/warfarin. The reduced burden of treatment will translate to greater patient adherence to their treatment plans and a positive effect on clinical outcomes.

Key words: Atrial fibrillation, Direct oral anticoagulant, Warfarin, Patient satisfaction

Atrial fibrillation (AF), the most common arrhythmia among the elderly, affects approximately 0.6% of the Japanese population. AF is an independent risk factor for stroke and death.1 Anticoagulation with vitamin K antagonist (VKA), such as warfarin, provides effective prophylaxis against stroke in AF patients, but the use of a VKA can be troublesome due to factors such as food-drug interaction, narrow therapeutic range, need for frequent monitoring of the international normalized ratio (INR), and slow onset of action. To overcome the limitations of VKAs, direct oral anticoagulants (DOACs) have been developed. Currently, DOACs are of two classes, with dabigatran being a direct thrombin inhibitor and rivaroxaban, apixaban, and edoxaban being factor Xa inhibitors. Recent randomized control trials have shown the benefit of these DOACs in reducing the risk of vascular events and bleeding complications in AF patients.2-5 Although DOACs are advantageous over VKAs/warfarin in terms of clinical convenience, whether Japanese patients given a DOAC are truly satisfied with their treatment remains unclear. Patient satisfaction remains an important factor that influences whether patients adhere to their care plan. Having access to the SAKURA AF Registry, we conducted a questionnaire-based prospective study to determine whether patients undergoing anticoagulant therapy are satisfied with their treatment.

Methods
Patient selection: Our investigation was conducted as a...
substudy of the SAKURA AF Registry (UMIN 000014420), which was set up to support multicenter prospective observational research by tracking clinical events in AF patients for at least 2 years and up to 4 years after their enrollment. Patients were enrolled between September 2013 and December 2015 and were eligible for inclusion if they were ≥ 20 years of age, nonvalvular AF had been diagnosed, and they were beginning or had already begun treatment with an anticoagulant drug for stroke prevention. From this Registry, patients to be included in our substudy were enrolled by clinicians at each of 40 (63%) institutions (2 cardiovascular centers, 14 affiliated hospitals or community hospitals, and 24 private clinics) in the Tokyo area. Patients were considered eligible for the substudy if they had been treated with an anticoagulant for > 3 months and if they had completed the treatment satisfaction questionnaires distributed upon their enrollment in the Registry. Analysis of the Registry data was approved by the Nihon University School of Medicine Itabashi Hospital Institutional Review Board (IRB) and the IRBs of the hospitals where patients were being treated, and all enrollees had provided written informed consent for their participation in the Registry. **Treatment satisfaction questionnaires:** Upon their enrollment in the Registry, patients were asked to complete two treatment satisfaction questionnaires: anticoagulation-specific Anti-Clot Treatment Scale (ACTS) and Treatment Satisfaction Questionnaire for Medication II (TSQM II), which is a widely used and translated generic patient instrument used to measure patient satisfaction with treatment, and the ACTS was again obtained at least 5 months after their enrollment. The Japanese version of ACTS and TSQM II has been translated into Japanese, and linguistic validation has been conducted by MAPI institute (Linguistic validation certificate available in file; Supplemental Figure). The scores obtained upon patients' enrollment in the Registry were viewed as baseline scores, and those obtained later were used to assess change in patient satisfaction with anticoagulation treatment.

The ACTS is a 17-item self-administered questionnaire designed to particularly measure patient satisfaction with anticoagulation treatment. Thirteen items address the burden of anticoagulation therapy (12 items on the so-called burdens scale plus 1 global question about burden), and four items address the benefits of anticoagulation therapy (three items on the so-called benefits scale plus one global question about benefits). The two global questions were not included in our calculation of scores. The previously validated psychometric properties of the ACTS are acceptability, scaling assumptions, reliability, validity, and responsiveness. Each of the total 15 items is scored on a 5-point Likert scale ranging from 1 (“not at all”), 2 (“a little”), 3 (“moderately”), 4 (“quite a bit”), and to 5 (“extremely”). Of the total 15 items, the 12 ACTS burdens items were reverse coded (scored from 5 to 1), but the three ACTS benefit items were coded (scored from 5 to 1), so that higher scores indicated greater patient satisfaction. The scores were totaled for each subscale to yield an ACTS burdens score ranging from 12 to 60 and an ACTS benefits score ranging from 3 to 15. In this study, “highly satisfied” was defined by a burdens score of ≥ 48 (indicating 4 [“quite a bit satisfied”] or 5 [“extremely satisfied”] out of all ACTS 12 burden items) and by a benefits score of ≥ 12 (indicating 4 [“quite a bit satisfied”] or 5 [“extremely satisfied”] out of all 3 ACTS benefit items). In accordance with the developers' guidelines for ACTS, if the patients responded to < 50% of the ACTS items, their responses were disqualified, whereas if the patients responded to ≥ 50%, person mean imputation was applied to each of the subscales.

The patients’ responses to the TSQM II completed upon enrollment were used as a benchmark, and their responses to the ACTS were evaluated alongside their responses to the TSQM II; we assumed correlation between the TSQM II and ACTS scores. The TSQM II covers four domains: effectiveness (two items), side effects (three items with an additional yes/no item), convenience (three items), and global satisfaction (two items). Each item for side effects was scored on a 5-point Likert scale ranging from 1 “a great deal,” 2 “quite a bit,” 3 “somewhat,” 4 “minimally,” to 5 “not at all.” Each item for effectiveness, convenience, and global satisfaction was scored on a 7-point Likert scale ranging from 1 “extremely dissatisfied,” 2 “very dissatisfied,” 3 “dissatisfied,” 4 “somewhat satisfied,” 5 “satisfied,” 6 “very satisfied,” to 7 “extremely satisfied.” Total scores in each domain were converted to a score between 0 and 100, with higher scores indicating greater satisfaction with treatment. In this study, “highly satisfied” was defined by an effectiveness, convenience, or global satisfaction score of ≥ 66.6 (indicating 5 “satisfied,” 6 “very satisfied,” or 7 “extremely satisfied” out of all 2 or 3 items for the three domains) and by a side effect score of 100 (indicating 5 “not dissatisfied at all” out of all three side effect items).

**Statistical analysis:** Numerical data are shown as mean ± standard deviation (SD), and categorical data are shown as the percentage and numbers of the patients. Variables were compared between the two main study groups, i.e., the DOAC and warfarin users, and/or among the dabigatran, rivaroxaban, and apixaban users. Differences in terms of patient characteristics between the two main study groups were analyzed by Student’s t-test or $\chi^2$, as appropriate. Differences in terms of the ACTS and TSQM II scores between these two groups were analyzed by Mann-Whitney U-test, those in terms of the ACTS and TSQM II scores among the dabigatran, rivaroxaban, and apixaban users were analyzed by the Kruskal-Wallis test and Steel-Dwass post hoc test. To reduce the effect of potential covariables in the observation study, we adjusted for the differences in the baseline characteristics using propensity score matching. Patient characteristics during Registry enrollment (age, sex, body mass index, AF type [paroxysmal versus persistent], hypertension, diabetes, vascular disease, congestive heart failure, prior stroke/transient ischemic attack (TIA), major bleeding, AF ablation, type of anticoagulant [DOAC versus warfarin], use of antiplatelet drug(s), use of NSAID(s), duration of therapy, and creatinine clearance) were entered into the model. On the basis of their propensity score, the DOAC and warfarin users were matched on a 1:1 basis with the nearest neighbor pair-matching algorithm with a 0.2-caliper width. Stepwise multiple regression modeling was also per-
signed ranks test was used to analyze change in the ACTS and that increase F by <0.1 were excluded. Wilcoxon increased the probability of F by at least 0.05 were included matching were entered into the model. Variables that in-
on the test scores. All covariables used in the propensity 
formed to assess the effects of the patient characteristics on the test scores. All covariables used in the propensity 
matching were entered into the model. Variables that in-
creased the probability of F by at least 0.05 were included 
and that increase F by <0.1 were excluded. Wilcoxon signed ranks test was used to analyze change in the ACTS  

### Table I. Patient Characteristics upon Enrollment in the SAKURA AF Registry per Study Group

| Medical history                  | DOAC users (n = 654) | Warfarin users (n = 821) | P-value* |
|----------------------------------|----------------------|--------------------------|----------|
| Age (years)                      | 71.8 ± 9.0           | 71.6 ± 9.2               | 0.7132   |
| Female                           | 156 (23.9)           | 175 (21.3)               | 0.2464   |
| Weight (kg)                      | 64.2 ± 13.3          | 64.1 ± 12.6              | 0.9318   |
| BMI (kg/m²)                      | 24.2 ± 3.7           | 24.0 ± 3.8               | 0.3000   |
| AF type                          |                      |                          |          |
| Paroxysmal AF                    | 231 (35.3)           | 260 (31.7)               |          |
| Persistent AF                    | 133 (20.3)           | 194 (23.6)               | 0.3176   |
| LS-PerAF                         | 286 (43.7)           | 360 (43.9)               |          |
| Not reported                     | 4 (0.6)              | 6 (0.9)                  |          |
| Hypertension                     | 469 (71.7)           | 628 (76.5)               | 0.0367   |
| Diabetes mellitus                | 146 (22.3)           | 207 (25.2)               | 0.1964   |
| Vascular disease                 | 78 (11.9)            | 125 (15.2)               | 0.0677   |
| Congestive HF                    | 132 (20.2)           | 219 (26.7)               | 0.0032   |
| Prior stroke/TIA                 | 76 (11.6)            | 99 (12.1)                | 0.7962   |
| Major bleeding                   | 9 (1.4)              | 9 (1.1)                  | 0.6267   |
| AF ablation                      | 48 (7.3)             | 54 (6.6)                 | 0.5666   |
| Antiplatelet drug (s)            | 91 (13.9)            | 179 (21.8)               | <0.0001  |
| NSAID (s)                        | 11 (1.7)             | 15 (1.8)                 | 0.8334   |
| CHADS2 score                     | 1.79 ± 1.18          | 1.91 ± 1.14              | 0.0495   |
| CHA2DS2-VASc score               | 2.94 ± 1.50          | 3.08 ± 1.50              | 0.0836   |
| Therapy duration (months)        | 12.2 (7.2-22.1)      | 58.1 (31.1-98.8)         | <0.0001  |
| CrCl (mL/minute)                 | 70.3 ± 28.2          | 65.9 ± 26.1              | 0.0018   |

Values are shown as mean ± SD, median and interquartile range, or n (%). *by Student’s t-
test, Mann-Whitney U-test, or χ² test, as appropriate. AF indicates atrial fibrillation; BMI, body mass index; LS-PerAF, long-standing persistent AF; HF, heart failure; TIA, transient ischemic attack; NSAID: non-steroidal anti-inflammatory drug; CHADS2, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and stroke; CHA2DS2-VASc, congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke, vascular disease, age = 65-74 years, and sex category; and CrCl, creatinine clearance.

### Table II. Mean Baseline Anti-Clot Treatment Scale (ACTS) and Treatment Satisfaction Questionnaire for Medication II (TSQM II) Scores Per Study Group

| ACTS                                                                                                                                                                                                 | DOAC users (n = 654) | Warfarin users (n = 821) | Difference: DOAC versus warfarin | P-value* |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|--------------------------|---------------------------------|----------|
| **ACTS**                                                                                                                                                                                               |                      |                          |                                 |          |
| Burdens                                                                                                                                                                                               | n = 645              | n = 797                   | 52.7 ± 6.9                      | 1.8 (1.1-2.5) | <0.0001 |
| Highly satisfied ≥ 48                                                                                                                                                                                  | 566 (87.8)           | 637 (79.9)                |                                 |          |
| Benefits                                                                                                                                                                                              | n = 641              | n = 793                   | 10.1 ± 3.2                      | -0.3 (-0.03-0.7) | 0.0513 |
| Highly satisfied ≥ 12                                                                                                                                                                                 | 227 (34.5)           | 317 (40.0)                |                                 | 0.0767   |
| **TSQM II**                                                                                                                                                                                            |                      |                          |                                 |          |
| Effectiveness                                                                                                                                                                                         | n = 640              | n = 807                   | 66.0 ± 15.0                     | -1.0 (-2.5-0.5) | 0.4222 |
| Highly satisfied ≥ 66.6                                                                                                                                                                                 | 430 (67.2)           | 551 (68.3)                |                                 | 0.6594   |
| Side effects                                                                                                                                                                                          | n = 605              | n = 768                   | 92.8 ± 14.4                     | 0.7 (-0.7-2.3) | 0.0666 |
| Highly satisfied ≥ 100                                                                                                                                                                                 | 457 (75.5)           | 540 (70.3)                |                                 | 0.0311   |
| Convenience                                                                                                                                                                                           | n = 642              | n = 809                   | 68.9 ± 14.5                     | -1.3 (-2.8-0.2) | 0.2804 |
| Highly satisfied ≥ 66.6                                                                                                                                                                                 | 454 (70.7)           | 588 (72.7)                |                                 | 0.4084   |
| Global satisfaction                                                                                                                                                                                   | n = 634              | n = 801                   | 66.0 ± 14.6                     | -1.3 (-2.9-0.2) | 0.4072 |
| Highly satisfied ≥ 66.6                                                                                                                                                                                 | 415 (65.5)           | 527 (65.8)                |                                 | 0.8943   |

Values are shown as mean ± SD or mean (confidence interval). *by Mann-Whitney U-test or χ² test, as appropriate.

scores (difference between the follow-up and baseline scores). The clinical significance of observed mean difference over time was interpreted in terms of statistical (P-value from independent sample) and clinical significance (Cohen’s d; effect size), calculated as the mean difference in scores at time point 1 to time point 2 divided by the
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Figure. Anti-clot treatment scale (ACTS) scores and treatment satisfaction questionnaire for the medication version II (TSQM II) scores of the dabigatran (DA; n = 241), rivaroxaban (Riv; n = 331), and apixaban (Api; n = 81) users. *P < 0.05 versus dabigatran by Kruskal-Wallis test plus Steel-Dwass post hoc test.

Results

Substudy patients and their characteristics: From the SAKURA AF Registry, 1475 patients treated with an anticoagulant drug were enrolled in our substudy. Of the total study patients, 654 (44.3%) were DOAC users (dabigatran, n = 241 [16.3%], rivaroxaban, n = 331 [22.4%], apixaban, n = 81 [5.5%], or edoxaban, n = 1 [0.1%]) and 821 (55.7%) were warfarin users. Characteristics of the study patients upon their enrollment in the Registry are shown per group in Table I. There was no difference between the DOAC and warfarin users in terms of age, sex, body weight, body mass index, and AF type. Overall, risk factors for stroke tended to be less prevalent, the CHADS\textsubscript{2} and CHA\textsubscript{2}-DS\textsubscript{2}-VASc scores to be lower, and creatinine clearance to be significantly better among the DOAC users than among the warfarin users. Concomitant use of antiplatelet drugs was less prevalent among the DOAC users than among the warfarin users. Duration of anticoagulant therapy was significantly shorter among the DOAC users than among the warfarin users.

ACTS scores: The baseline ACTS scores are shown per study group in Table II. The burdens scores were significantly higher (54.5 ± 6.3 versus 52.7 ± 6.9, P < 0.0001) and "highly satisfied" (defined by scores ≥ 48) was often obtained (87.8% versus 79.9%, P < 0.0001) among the DOAC users than among the warfarin users, but the baseline benefits scores among the DOAC users tended to be lower (9.8 ± 3.1 versus 10.1 ± 3.2, P = 0.0513) and "highly satisfied" (defined by scores ≥ 12) to be less prevalent than those among the warfarin users (34.5% versus 30.0%; P = 0.0767). There were no differences in terms of the burdens and benefits scores among the dabigatran, rivaroxaban, and apixaban users (P > 0.05; Figure). Stepwise multiple regression analysis of the patient characteristics in relation to ACTS scores revealed significant association between the use of a DOAC and treatment satisfaction and between hypertension and treatment satisfaction per the burdens scale (β = 0.135, P < 0.001 and β = 0.070, P = 0.007, respectively), but only prolonged anticoagulation therapy positively correlated with satisfaction per the benefits scale (β = 0.068, P = 0.011; Table III).

SD of the time point 1 score. Effect sizes were interpreted as follows: 0.2 (small change), 0.5 (moderate change), and 0.8 (large change). All statistical analyses were performed using JMP 11.0.2 (SAS Institute Inc, Cary, NC, USA) or IBM SPSS Statistics for Windows (version 24.0; IBM Corp, Armonk, NY, USA). P < 0.05 was considered statistically significant.
TSQMI II scores: There was no difference in terms of the baseline effectiveness, convenience, and global satisfaction scores between the DOAC and warfarin users, but the side effects scores tended to be higher (93.6 ± 13.7 versus 92.8 ± 14.4, *P* = 0.0666) and the prevalence of the “highly satisfied” for side effects significantly higher among the DOAC users than those among the warfarin users (75.5% versus 70.3%, *P* = 0.0311; Table II). There was no difference in terms of the baseline effectiveness, side effects, or global satisfaction scores (*P* > 0.05) among the dabigatran, rivaroxaban, and apixaban users, but the convenience scores were higher among the rivaroxaban users than those among the dabigatran or apixaban users (69.0 ± 14.0 versus 66.2 ± 15.4 or 65.9 ± 13.0, respectively, *P* = 0.0386 and *P* = 0.0731; Figure). Stepwise multiple regression analysis revealed significant positive correlation or association of age (β = 0.066, *P* = 0.014), vascular disease (β = 0.062, *P* = 0.020), and hypertension (β = 0.053, *P* = 0.046) with the effectiveness scores; of female (β = 0.062, *P* = 0.022) and persistent AF (β = 0.055, *P* = 0.042) with the side effects scores; of age (β = 0.087, *P* = 0.001) and a history of AF ablation (β = 0.064, *P* = 0.017) with the convenience scores; and of age (β = 0.093, *P* < 0.001) and hypertension (β = 0.083, *P* = 0.002) with the global satisfaction scores (Table III).

Propensity score matching cohort: Propensity score matching yielded 258 matched pairs of the patients. There were no longer any significant differences between the DOAC and warfarin users with regard to the baseline characteristics (Table IV). For the matched study group, baseline ACTS burdens scores remained to be significantly higher (54.1 ± 6.3 versus 52.9 ± 6.5, *P* = 0.0213) and the highly satisfied for burdens to be more prevalent among the DOAC users than among the warfarin users (87.0% versus 80.3%, *P* = 0.0413), but there was no difference in terms of the baseline ACTS benefits scores and prevalence of the highly satisfied for benefits between the DOAC and warfarin users. The baseline TSQMI II effectiveness, convenience, and global satisfaction scores did not differ between the DOAC and warfarin users, except for the higher prevalence of the “highly satisfied” for effectiveness among the DOAC users (Table IV).

Changes in ACTS scores: Of the total 1475 study patients, 513 (34.8%) completed the follow-up ACTS questionnaires 11.8 ± 5.8 months after their enrollment in the Registry. During the follow-up, the anticoagulant drugs used did not change for 206 of the DOAC users and for 273 of the warfarin users (Table V). In these two groups, the mean ACTS burdens and benefits scores did not significantly change over time (*P* > 0.05), regardless of the type of anticoagulant drug used, but the ACTS burdens scores remained significantly higher for the DOAC users than for the warfarin users (*P* < 0.0001). DOAC was changed to warfarin for six DOAC users, and warfarin was changed to a DOAC for 28 warfarin users. In these two groups, the mean ACTS burdens and benefits scores did not significantly change over time (*P* > 0.05), regardless of the change in the anticoagulant drug used, but the ACTS burdens score marginally increased with a modest effect size among the patients who switched from warfarin to a DOAC (from 53.4 ± 5.4 to 55.1 ± 5.5, *P* = 0.140; effect size, 0.31; Table V).

**Discussion**

The study results can be summarized as follows: (1) The ACTS burden scores were significantly higher among the DOAC users than those among the warfarin users, and the higher scores were independent of age, sex, and other clinical variables. The ACTS benefits scores were somewhat higher among the warfarin users than among the DOAC users, and prolonged anticoagulant therapy was the strongest determinant of satisfaction shown on the benefits scale. (2) Although the TSQMI II scores did not differ between the DOAC and warfarin users, positive associations were found for side effects (female), effectiveness (age), convenience (age), and global satisfaction (age). (3) After the propensity score-matched group pairs, the ACTS burden scores remained to be significantly higher among the DOAC users than among the warfarin users. (4) The ACTS scores did not significantly change over time, and the satisfaction indicated by the burdens scores of the DOAC users remained greater than that of the warfarin users.

**Satisfaction with treatment (DOACs versus warfarin/VKAs):** The greater satisfaction indicated by the DOAC users through their burdens scores persisted even after ad-
among the DOAC users than among the warfarin users.

and the ACTS benefits scores were somewhat lower
highly satisfied with anticoagulant therapy for benefits,
note, however, that only 34.5%-40% of the patients were
associated with traditional VKAs, is reduced.12) We did
tions, and risk of fatal bleeding, in comparison with that
there is no need for INR monitoring or drug/food restric-
tion for covariates. There have been no randomized
trials that compared satisfaction between the AF patients
given DOAC and those given warfarin/VKA by the ACTS
questionnaire. Because of the different patient background
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Table IV. Patient Characteristics upon Enrollment in the SAKURA AF Registry Per
Matched Study Group

|                      | DOAC users (n = 258) | Warfarin users (n = 258) | P-value* |
|----------------------|----------------------|--------------------------|----------|
| Age (years)          | 71.3 ± 8.5           | 71.6 ± 9.4               | 0.7024   |
| Female               | 58 (22.5)            | 62 (24.0)                | 0.2464   |
| Weight (kg)          | 62.9 ± 12.7          | 63.6 ± 13.1              | 0.5621   |
| BMI (kg/m²)          | 23.7 ± 3.5           | 24.0 ± 4.0               | 0.3277   |
| AF type              |                      |                          |          |
| Paroxysmal AF        | 104 (40.3)           | 104 (40.3)               |          |
| Persistent AF        | 46 (17.8)            | 48 (18.6)                | 0.9698   |
| LS-PerAF             | 108 (41.9)           | 106 (41.1)               |          |
| Medical history      |                      |                          |          |
| Hypertension         | 187 (72.5)           | 199 (77.1)               | 0.2237   |
| Diabetes mellitus    | 62 (24.0)            | 61 (23.6)                | 0.9177   |
| Vascular disease     | 43 (16.7)            | 36 (14.0)                | 0.3921   |
| Congestive HF        | 69 (26.7)            | 68 (26.4)                | 0.9206   |
| Prior stroke/TIA     | 29 (11.2)            | 31 (12.0)                | 0.7836   |
| Major bleeding       | 4 (1.6)              | 2 (0.8)                  | 0.4115   |
| AF ablation          | 25 (9.7)             | 18 (7.0)                 | 0.2649   |
| Antiplatelet drug(s) | 61 (23.6)            | 46 (17.8)                | 0.1034   |
| NSAID(s)             | 4 (1.55)             | 7 (2.7)                  | 0.3605   |
| CHADS2 score         | 1.85 ± 1.16          | 1.90 ± 1.13              | 0.5439   |
| CHA2DS2-VASc score   | 3.03 ± 1.44          | 3.08 ± 1.45              | 0.7155   |
| Therapy duration     | 21.3 (10.9-33.2)     | 22.8 (13.2-36.2)         | 0.1978   |
| CrCl (mL/minute)     | 65.9 ± 24.1          | 67.6 ± 26.0              | 0.4343   |
| ACTS                  |                      |                          |          |
| Burdens              | 54.1 ± 6.3           | 52.9 ± 6.5               | 0.0213   |
| Highly satisfied ≥ 48| 221 (87.0)           | 204 (80.3)               | 0.0413   |
| Benefits             | 9.8 ± 3.1            | 9.7 ± 3.5                | 0.7708   |
| Highly satisfied ≥ 12| 98 (38.7)            | 89 (35.2)                | 0.4072   |
| TSQM II              |                      |                          |          |
| Effectiveness        | 65.2 ± 11.6          | 65.3 ± 16.0              | 0.4535   |
| Highly satisfied ≥ 66.6| 178 (70.6)          | 156 (61.7)               | 0.0331   |
| Side effects         | 92.6 ± 14.4          | 92.6 ± 14.5              | 0.4291   |
| Highly satisfied = 100| 176 (74.6)          | 173 (70.3)               | 0.2966   |
| Convenience          | 66.8 ± 13.5          | 68.8 ± 14.6              | 0.0575   |
| Highly satisfied ≥ 66.6| 177 (69.4)          | 190 (74.2)               | 0.2272   |
| Global satisfaction  | 64.4 ± 14.3          | 65.6 ± 15.3              | 0.9385   |
| Highly satisfied ≥ 66.6| 167 (65.8)          | 163 (64.2)               | 0.7099   |

Values are shown as mean ± SD, median and interquartile range, or n (%). *by Student’s t-test, Mann-Whitney U-test, or χ2 test, as appropriate. Abbreviations are shown in Table I.

that investigated the satisfaction of DVT/PE patients taking
rivaroxaban against that of patients taking a traditional
VKA would provide additive insight into understanding
treatment satisfaction of anticoagulant drugs.13,14) In these
two trials, greater satisfaction was reported via ACTS bur-
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treatment satisfaction of anticoagulant drugs.
find that prolonged therapy was the strongest predictor of a positive ACTS benefits score. Taken together, our data suggest that the safety and ease of DOAC use can improve patient satisfaction with anticoagulation therapy, but clinicians should maintain patient education for the benefit of DOACs on stroke prophylaxis. This education would be important especially at the time of the DOAC initiation. Reducing the patient-reported burdens of anticoagulation therapy and constant patient education of the benefit for stroke prophylaxis may increase adherence to treatment and improve clinical outcomes because of the strong relation between patient satisfaction and adherence to treatment.7,18)

Disappointingly, we did not see a substantial difference in the TSQM II scores between the DOAC and warfarin users. Only the side effects scores differed, and the difference was quite small. The apparently reduced side effects among the DOAC users may in part explain the greater satisfaction of the DOAC users reflected by their ACTS burdens scores. In another reported study of a randomized trial that investigated the clinical outcome after cardioversion in nonvalvular AF patients given rivaroxaban versus patients given a VKA, the TSQM II effectiveness, convenience, and global satisfaction scores were higher for rivaroxaban users.17) In the two studies noted above, DVT/PE patients treated with rivaroxaban rather than a VKA also reported statistically greater satisfaction with treatment, as reflected across all four TSQM II domains.5,14) We noted, however, that even in randomized trials, patients are selected for treatment with a new drug on the basis of strict criteria and may, therefore, naturally favor the new drug.

In our study, most of the TSQM II scores positively correlated with age. The prevalence of risk factors for stroke, such as hypertension, diabetes mellitus, and coronary heart disease, increases with age; thus, advanced age is the strongest determinant for stroke.2–5) Therefore, elderly patients may live with a fear of stroke/TIA and may thus be likely to report that they are satisfied with treatment, regardless of the anticoagulant drug being administered. Detailed anticoagulation therapy-specific instruments such as the ACTS and SAFUCA questionnaire can optimize this differentiation in real-world clinical practice.7,18)

Patient satisfaction with dabigatran, rivaroxaban, or apixaban: Most of the recent reports exploring patient satisfaction with anticoagulant treatment compared treatment with rivaroxaban vs. VKA/warfarin. Ours may be one of the first studies to examine patient satisfaction with respect to each of three DOACs (dabigatran, rivaroxaban, and apixaban). There were no between-group differences in the ACTS burdens or benefits scores or the TSQM II effectiveness, side effects, and global satisfaction scores, suggesting that patients’ satisfaction levels for burdens were consistent, regardless of which DOAC they were taking. The higher TSQM II convenience scores reported by rivaroxaban users may have been the result of the once-daily dosing regimen.19) The once-daily regimen may foster medication adherence can prevent stroke and in turn result in patient satisfaction.

Patient satisfaction over time: The greater satisfaction reflected in the DOAC patients’ ACTS burdens scores did not change during the mean follow-up period of 11.8 months. These results were consistent with the follow-up results of other observational studies conducted in nonvalvular AF patients20,21) and of the EINSTEIN-DVT/PE studies,15,16) but as noted, we did not find any difference in terms of the ACTS benefits scores. Our results together with other prior reports may, in part, support reproducibility or reliability of the ACTS scores for the patient satisfaction assessment in Japanese AF patients given anticoagulant drugs. Patients’ satisfaction with treatment would also depend on their personality. Therefore, it is thought to be important to assess treatment satisfaction in those who had undergone a switch from warfarin to DOAC and vice versa. In our study, the ACTS burdens scores marginally increased, and its effect size was modest among the patients for whom warfarin was switched to a DOAC, although it was not statistically significant possibly because of a small number of patients. This result is consistent with those previously reported in AF patients.20,21) In the two previously reported observational studies, switching from a VKA to rivaroxaban resulted in statistically and clinically significant improvements in the ACTS burdens and benefits scores.

Limitations: Studies based on a real-world patient regis-

| ACTS scores | Baseline | Follow-up | Difference | P-value* | Effect size |
|-------------|----------|-----------|------------|----------|-------------|
| Burdens     |          |           |            |          |             |
| DOAC-to-DOAC (n = 202) | 54.9 ± 5.4† | 55.1 ± 5.7† | 0.1 ± 5.5 | 0.4345 | 0.02 |
| DOAC-to-WF (n = 6) | 52.2 ± 9.4 | 52.7 ± 8.2 | 0.5 ± 11.6 | 0.9062 | 0.10 |
| WF-to-WF (n = 265) | 52.2 ± 6.9 | 52.5 ± 7.1 | 0.3 ± 6.4 | 0.8933 | 0.05 |
| WF-to-DOAC (n = 28) | 53.4 ± 5.4 | 55.1 ± 5.5 | 1.7 ± 7.6 | 0.1400 | 0.31 |
| P-value** | 0.0002 | < 0.0001 | 0.3142 |          |             |
| Benefits    |          |           |            |          |             |
| DOAC-to-DOAC (n = 198) | 9.6 ± 2.9 | 9.7 ± 3.0 | 0.3 ± 3.4 | 0.3299 | 0.10 |
| DOAC-to-WF (n = 6) | 8.5 ± 2.8 | 10.8 ± 3.2 | 2.3 ± 3.4 | 0.1875 | 0.82 |
| WF-to-WF (n = 265) | 10.1 ± 3.3 | 9.8 ± 3.1 | 0.3 ± 3.9 | 0.2478 | 0.09 |
| WF-to-DOAC (n = 27) | 10.0 ± 3.0 | 9.3 ± 3.4 | 0.7 ± 4.5 | 0.5118 | 0.23 |
| P-value** | 0.0632 | 0.7591 | 0.1970 |          |             |

ACTS indicates anti-clot treatment scale; DOAC, direct oral anticoagulant; and WF, warfarin. *by Wilcoxon rank sum test. **for differences between the 4-groups as analyzed by Kruskal-Wallis test. †P < 0.05 versus WF-to-WF group by Steel-Dwass post hoc test.
try have several limitations. Because it is up to clinicians to distribute questionnaires during routine clinical practice, it is possible that some patients are missed. It is also possible that patients who do complete the questionnaires represent a selection bias simply by virtue of the fact that those who respond, in comparison to those who do not respond, may view their treatment more favorably or may adhere to treatment and follow-up more faithfully. Therapy duration or other patient characteristics between the warfarin and DOAC users may have influenced our results. Nonetheless, the greater satisfaction of the ACTS burdens scores among the DOAC users persisted even after adjustment for covariates or after propensity matching method, and the ACTS burdens scores marginally increased among the patients for whom warfarin was switched to a DOAC. These support that the DOAC users had at least a greater satisfaction of the burden of treatment.

Conclusion

The results of our study indicate that we can expect greater satisfaction with anticoagulation treatment in patients given a DOAC than in those given warfarin in terms of the burden of treatment, but it was not evident in the benefit for prophylaxis against stroke. The reduced burden of DOACs and constant patient education for the benefit of stroke prophylaxis will lead to greater adherence of patients to their treatment plan and thus have a positive effect on clinical outcomes.

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Disclosures

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Supplemental File
Supplemental Figure.
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