Prescribing Patterns and Preference Attributes of Novel Oral Anticoagulants in Atrial Fibrillation and Venous Thromboembolism in Real-World Practice in China: A Nationwide Physician Survey

Wang R[1], Li J[2], Du J[3], Higashiyama H[3], Huang Z[4], Ye X[1], Yang M[5]

[1]Daiichi Sankyo Inc, Basking Ridge, NJ, USA, [2]Happy Life Technology, Boston, MA, USA, [3]Daiichi Sankyo Holdings CO., LTD, Shanghai, China, [4]Cornell University, New York, NY, USA, [5]Happy Life Technology, Short Hills, NJ, USA

Background

In recent years, four new oral anticoagulants (NOACs) have been approved and listed in the catalog of medicines covered by national medical insurance system in China, including rivaroxaban (approved in 2009), edoxaban (approved in 2018), apixaban (approved in 2013), and dabigatran (approved in 2013). However, physicians' prescribing patterns and preference for NOACs in patients with atrial fibrillation (AF) and venous thromboembolism (VTE) in China are unclear.

Objective

The goal of this nationwide physician survey is to gain a comprehensive understanding of the current prescribing patterns and preference for NOACs in the treatment of AF and VTE in China, to ultimately improve patient care and inform healthcare decision making and relevant guidelines.

Methods

This was a national quantitative and qualitative survey. Totally 50 physicians from 27 tertiary hospitals (comprehensive, referral, general hospitals with the highest grade [e.g., with a bed capacity exceeding 500], which can be further subdivided into three subsidiary levels: A, B and C based on size, medical equipment, medical quality, etc., with A being the highest level) in China were interviewed. A polit survey with three physicians were performed prior the formal survey to optimize the questionnaire design. The survey collected and analyzed information on the prescription pattern and factors that influence the use of NOACs. The main questions included the proportion and reasons for prescribing NOACs and warfarin for AF/VTE patients for the first time in the past three months, factors impacting drug selection, and patient adherence to NOACs, etc. The selected doctors were all from tertiary hospitals, currently treating at least five AF or VTE patients in outpatient setting per week, and familiar with the use of NOACs.

Results were analyzed using descriptive statistics. For categorical variables, the number and percentage of observations were counted for each variable. For continuous variables, the number of observations, mean, etc. were calculated. Results were analyzed separately for physicians treating AF or VTE.

Eligibility criteria:

1. A physician with the title of attending physician or above
2. Working in a designated tertiary hospital
3. Aged between 30 and 55 years old
4. Having graduate (or higher-level) degree
5. At least two half-day outpatient clinics per week
6. Treating at least five AF or VTE patients in outpatient setting per week for the AF or VTE cohort respectively
7. Familiar with the use of NOACs and warfarin

Number of physicians:
Formal survey: 50 physicians (10 chief physicians, 20 deputy chief physicians and 20 attending physicians)

Survey format: One-time online/in-person survey, one hour each

Results

Physicians

	AF (N=30)	VTE (N=20)
Gender		
Male	40%	80%
Female	60%	20%
Department		
Cardiology	100%	5%
Vascular Surgery	0%	75%
Respiratory Medicine	0%	15%
Thoracic Surgery	0%	5%
Other	0%	0%
Hospital Level		
Tertiary, Level A	96.7%	100%
Tertiary, Level B	3.3%	0%
Age		
30-39	36.7%	35%
40-49	23.3%	45%
50-55	40%	20%
Education		
Master	40%	25%
Doctoral	60%	75%

Title		
Chief Physician	20%	20%
Deputy Chief Physician	40%	45%
Attending Physician	40%	35%
Years of Experience		
≤10	30%	25%
11-20	30%	50%
21-30	40%	25%
Average Time of Seeing Patients (Hours/Week)		
[8-16]	30%	75%
[17-32]	66.7%	25%
[33-56]	3.33%	0%
Average Number of AF/VTE Patients in Outpatient Setting per Week		
<30	76.7%	85%
≥30	23.3%	15%
Average Number of AF/VTE Patients in Inpatient Setting per Week		
<5	40%	45%
≥5	60%	55%

Table 1. Basic Information of AF & VTE Physicians

- Table 1a shows the basic information of interviewed physicians treating AF patients, including gender, department, hospital level, age, education level, professional title, years of experience, and patient volume. All of the physicians (except one) surveyed were from Tertiary, Level A hospitals. All physicians treating AF were from the cardiology department, and 75% of the physicians treating VTE were from the vascular surgery department.

AF Results: Drug Choice & Drug Choice Considerations

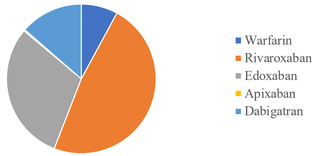

Figure 1a. Physician responses for initial choice of warfarin or NOACs in AF patients in the past 3 months

- Figure 1a shows physician's initial choice of drugs in AF patients in the past three months. Among warfarin and the four NOACs, rivaroxaban was the mostly used, accounting for 48%. Edoxaban ranked the second, accounting for 30.2%. Following that were dabigatran, warfarin, and apixaban, accounting for 13.6%, 7.9%, and 0.3% respectively.
- Rivaroxaban was used the most as it was the first NOAC entering hospitals in China; therefore, physicians had more experience with it. Moreover, it had a generic version in China which was cheaper compared to other NOACs. There was some evidence supporting the use of rivaroxaban in patients with AF and coronary heart diseases, according to some physicians surveyed.
- Edoxaban ranked the second in this survey mainly due to its abundant clinical trial and real-world evidence in Asian population, evidence supporting its low dose use (e.g., in patients with renal impairment or with low body weight), and some patients' preference for imported drugs. However, because it was relatively new compared to other NOACs, physicians had less experience with it.
- Dabigatran was comparably inconvenient as it needed to be taken twice a day. Moreover, it could lead to higher risk of bleeding and more gastrointestinal adverse events comparing to other NOACs.
- Warfarin was mostly used in patients with heart valve disease or other conditions where NOACs were not indicated for. Due to its cheap price and long history, some patients may still choose it.
- Apixaban was not available in most hospitals. It only accounted for 0.3% in the drug choice, due to its no or short supply in hospitals, or physician's unfamiliarity with the drug.

Factors for Drug Choice	Rank*	Rivaroxaban ^N=30	Edoxaban^ N=29	Apixaban^ N=7	Dabigatran^ N=30
Reduced incidence of stroke	1 (2.17)	3.69	3.52	3	3.54
Low risk of bleeding	1 (2.17)	2.98	3.55	3.25	3.25
High-quality evidence, including clinical trials, real-world evidence, etc.	3 (2.90)	3.79	3.29	3.64	3.57
Convenience	4 (5.33)	3.83	3.78	2.83	2.65
Low risk of non-bleeding adverse reactions	5 (5.43)	3.71	3.66	3.17	3
Personal experience or peer recommendations	6 (6.30)	3.63	3.39	2.71	3.19
Low drug price/little health insurance reimbursement restriction	7 (6.37)	3.62	3.07	2.9	3.08
Few drug-food or drug-drug interactions	8 (6.80)	3.48	3.45	3.26	3.26
Adequate supply in hospital	9 (8.23)	3.57	3.55	2.25	3.31
High patient acceptance	10 (8.47)	3.46	3.28	2.92	3.2

Table 2a. Factors influencing physician's choice of NOACs for patients with AF
Notes: Mean in brackets. If the mean is the same, the further decimal digits decided the rank.
*The lower the mean is, the more important the factor is.
^A higher mean indicates a higher score on a factor.
#Not all physicians scored all the factors due to lack of experience or knowledge for some factors.

- Table 2a shows factors that may impact physician's choice of NOACs for AF patients. Physicians were asked to rank the ten factors and then score on a scale of 0-4 for each of the factors for the four NOACs.
- The top three factors that could influence physician's drug choice were reduced incidence of stroke, low risk of bleeding, and high-quality evidence. Rivaroxaban had some advantages in high-quality evidence and price. Edoxaban was scored the highest for low risk of bleeding. Dabigatran had the lowest score for convenience, and apixaban had the lowest score for adequate supply in hospital.

AF Results: Patient Adherence and Other

- The proportion of patients who completely adhered to NOACs ranged from 65% to 83%. Less than 6% of the patients completely did not adhere to NOACs.
- The top three factors impacting patient's adherence to NOACs were patient's knowledge about the disease, risk of bleeding and drug convenience.
- 86.7% of the physicians thought that QD or BID would influence their decision in prescribing drugs.

VTE Results: Drug Choice & Drug Choice Considerations

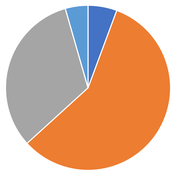

Figure 1b. Physician responses for initial choice of warfarin or NOACs in VTE patients in the past three months

- Figure 1b shows physician's initial choice of drugs in VTE patients in the past three months. Among warfarin and the four NOACs, Rivaroxaban was the mostly used, accounting for 57.6%. Edoxaban ranked the second, accounting for 32.3%. Warfarin and dabigatran ranked the third and fourth, accounting for 5.66% and 4.45% respectively. Apixaban was not used (0%).
- The distribution of drug choices and the underlying reasons were very similar to those given by physicians treating AF patients.
- Dabigatran was originally indicated for AF, and later expanded for VTE; hence, physicians in the vascular surgery department had less experience with it comparing to those in the cardiology department.
- No physician treating VTE had prescribed apixaban due to no current supply in hospital.

Factors for Drug Choice	Rank*	Rivaroxaban^ N=20	Edoxaban^ N=20	Apixaban^ N=3#	Dabigatran^ N=11#
Low risk of bleeding	1 (1.95)	3.61	3.54	3.67	3.18
High-quality evidence, including clinical trials, real-world evidence, etc.	2 (2.47)	3.95	3.38	2.75	3.14
Reduced incidence of VTE	3 (4.95)	3.67	3.47	3	3.45
Low risk of non-bleeding adverse reactions	4 (5.16)	3.61	3.76	3.5	3.45
Convenience	5 (5.37)	3.49	3.89	3.5	2.86
Personal experience or peer recommendations	6 (5.74)	3.76	3.32	2.33	2.55
Few drug-food or drug-drug interactions	7 (5.79)	3.45	3.87	3.8	3.85
Low drug price/little health insurance reimbursement restriction	8 (7.11)	3.37	3.11	NA	2.92
Adequate supply in hospital	9 (7.95)	3.21	3.89	NA	3.44
High patient acceptance	10 (8.37)	3.84	3.08	1.5	3.06

Table 2b. Factors influencing physician's choice of NOACs for patients with VTE
Notes: Mean in brackets. If the mean is the same, the further decimal digits decided the rank.
*The lower the mean is, the more important the factor is.
^A higher mean indicates a higher score on a factor.
#The responses may be based on evidence or guideline recommendations. Not all physicians scored all the factors due to lack of experience or knowledge for some factors.

- Table 2b shows physician's considerations when prescribing drugs to VTE patients. Physicians were asked to rank the ten factors and scored on a scale of 0-4 for each of them for the four NOACs.
- The top three factors that could influence physician's drug choice were low risk of bleeding, high-quality evidence, and reduced incidence of stroke. The scores of NOACs were similar to AF.

AF Results: Dose Selection

	Rivaroxaban N=30	Edoxaban N=29	Apixaban N=3	Dabigatran N=25
Low dose	10 mg QD: 24.8% 15 mg QD: 50.7%	30 mg QD: 50.5% 15 mg QD: 1.5%	2.5 mg QD: 60%	110 mg BID: 79.4%
High dose	20 mg QD: 24.5%	60 mg QD: 48%	5 mg QD: 40%	150 mg BID: 20.6%

Table 3. Physician responses for initial choice of low dose vs high dose NOACs in AF patients

- The proportion of physicians' initial choice of low dose and high dose NOACs ranged from to 52% (edoxaban) and 79.4% (dabigatran), and 20.6% (dabigatran) to 48% (edoxaban) respectively.
- The reasons of selecting low dose NOACs were similar in the four drugs, including:
  - patients with high risk of bleeding, impaired renal function, older age, or low body weight

VTE Results: Patient Adherence and Other

- The proportion of patients who completely adhered to NOACs ranged from 79.72% to 95%. Less than 3% of the patients completely did not adhere to NOACs. However, only very few (N<5) physicians provided response to BID NOACs (apixaban and dabigatran); therefore, the results could be biased. Patients taking rivaroxaban had to change dose (e.g., day 1- day 22: 15mg BID, day 22 and later: 20mg QD), leading to missed doses sometimes. Physicians responded that on average 88.8% of patients with VTE completely adhered to edoxaban.
- The top three factors impacting patient's adherence to NOACs were drug convenience, patient's knowledge about the disease, and drug price.
- All of the physicians thought that QD or BID would influence their decision in prescribing drugs.

Discussion

There are some limitations of the survey:

- Most physicians do not have experience with apixaban as it has no or very short supply in their hospitals. Hence, the results may be biased because there was little data for apixaban and the responses may be based on clinical evidence or guidelines.
- Some physicians may prefer older NOAC (such as rivaroxaban or dabigatran) than newer NOAC (such as edoxaban) due to personal experience or patient's preference. The treatment pattern may change over time.
- Most physicians are from the same department, e.g., cardiology for AF and vascular surgery for VTE. It is because only a few physicians from other departments could meet the criteria of treating at least five AF or VTE patients in outpatient setting per week. For example, patients with PE often visit the emergency department or the department of oncology department first, before being transferred to the department of respiratory medicine. Patients from the same department may have similar characteristics. For example, in some hospitals, the department of vascular surgery is not equipped for PE-related surgeries. Physicians could still prescribe NOACs to patients with PE; however, if a patient with PE needs surgery, the patient would be transferred to the department of thoracic surgery, etc.
- The surveyed physicians are all from Tertiary, Level A hospitals in China. Physicians' prescribing patterns and preference for NOACs may be different in lower level hospitals.

Conclusion

The survey outlined the prescribing patterns and preference for NOACs in the treatment of AF and VTE in China. A real-world study is needed to have a more thorough understanding of treatment pattern and preference attributes (e.g., effectiveness, safety, HCRU, and cost) of NOACs in AF or VTE, to better improve patient care and inform health care decision making and guidelines.