Atrial Fibrillation Better Care Pathway Adherent Care Improves Outcomes in Chinese Patients With Atrial Fibrillation

Yutao Guo, MD,a,b Jacopo F. Imberti, MD,b,c Agnieszka Kotalczyk, MD,b,d Yutang Wang, MD,e,* Gregory Y.H. Lip, MD,a,b,f,* on behalf of the ChiOTEAF Registry Investigators

ABSTRACT

BACKGROUND Atrial fibrillation (AF) is a complex disease associated with comorbidities and adverse outcomes. The Atrial fibrillation Better Care (ABC) pathway has been proposed to streamline the integrated and holistic approach to AF care.

OBJECTIVES This study sought to evaluate patients’ characteristics, incidence of adverse events, and impact on outcomes with ABC pathway-adherent management.

METHODS The study included consecutive AF patients enrolled in the nationwide, ChioTEAF registry (44 centers, 20 Chinese provinces from October 2014 to December 2018), with available data to evaluate the ABC criteria and on the 1-year follow-up.

RESULTS A total of 3,520 patients (mean age 73.1 ± 10.4 years, 43% female) were included, of which 1,448 (41.1%) were managed as ABC pathway adherent. The latter were younger and had comparable CHA2DS2-VASc and lower HAS-BLED (mean 71.7 ± 10.3 years of age vs 74.1 ± 10.4 years of age; P < 0.01; 3.54 ± 1.60 vs 3.44 ± 1.70; P = 0.10; and 1.95 ± 1.10 vs 2.12 ± 1.20; P < 0.01, respectively) scores compared with ABC-nonadherent patients. At 1-year follow-up, patients managed adherent to the ABC pathway had a lower incidence of the primary composite outcome of all-cause death or any thromboembolic event (1.5% vs 3.6%; P < 0.01) as compared with ABC-nonadherent patients. On multivariate analysis, ABC pathway-adherent care was independently associated with a lower risk of the composite endpoint (OR: 0.51; 95% CI: 0.31-0.84).

CONCLUSIONS Adherence to the ABC pathway for integrated care in a contemporary nationwide cohort of Chinese AF patients was suboptimal. Clinical management adherent to the ABC pathway was associated with better outcomes.

© 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Oral anticoagulation (OAC) with either warfarin or direct OACs represents the cornerstone of management for patients with atrial fibrillation (AF), given the important benefits in preventing stroke and all-cause mortality. However, AF often coexists with several cardiovascular and noncardiovascular risk factors and comorbidities, increasing the risk of heart failure, dementia, and death. Indeed, stroke only accounts for 1 in 10 AF-related deaths, while cardiovascular causes account for $\geq 7$ in 10 deaths.

The multifaceted and complex nature of AF requires a paradigm shift toward a holistic and multidisciplinary approach to improve overall patient outcomes. Preliminary reports suggested that an integrated care approach to AF management reduced cardiovascular hospitalizations and all-cause mortality, but the implementation of these models in everyday clinical practice was limited.

More recently, the ABC (Atrial Fibrillation Better Care) pathway was proposed as a decision-making strategy streamlining the multidisciplinary and integrated approach to AF care, with the potential to simplify the step-by-step evaluation and holistic care of patients with AF. The ABC pathway refers to avoid stroke with anticoagulation (A criterion), better symptom management with patient-centered and symptom-directed decisions on rate or rhythm control (B criterion), and comorbidity and cardiovascular risk factor management, including lifestyle changes (C criterion). It is designed to improve clinicians’ awareness and management of AF patients.

Several reports have confirmed the benefits of the ABC pathway-adherent management in different clinical settings and patients’ populations. However, no real-world study was explicitly performed in the Chinese population. To address this knowledge gap, we retrospectively evaluated the ABC pathway-adherent management and its impact on clinical outcomes in a contemporary Chinese nationwide cohort of patients with AF.

**METHODS**

The ChiOTEAF (Optimal Thromboprophylaxis in Elderly Chinese Patients with Atrial Fibrillation) registry was a prospective, observational, large-scale multicenter registry conducted between October 2014 and December 2018 in 44 sites from 20 provinces in China. A detailed description of the study design has been previously published. All patients enrolled were consecutive, had electrocardiographically documented clinical AF within 12 months before enrollment, and provided written informed consent. Follow-up was performed up to 3 years after inclusion. Data were collected at enrollment and follow-up visits by local investigators.

The ChiOTEAF registry was approved by the Central Medical Ethics Committee of Chinese PLA General Hospital, Beijing, China (approval # S2014-065-01) and local Institutional Review Boards.

Variables included in the registry and their definitions were designed to match the EORP-AF (EURObservational Research Programme Atrial Fibrillation) Long-Term General Registry (Supplemental Methods). The thromboembolic (TE) risk was defined according to the CHA$_2$DS$_2$-VASc score and the bleeding risk according to the HAS-BLED score.

The ABC pathway was retrospectively evaluated according to its original definition. The A criterion is defined as avoid stroke with anticoagulation. Patients qualified for the A criterion if treated with OACs adequately to their TE risk. In particular, patients with a CHA$_2$DS$_2$-VASc score $\geq$ if male or $\geq 2$ if female receiving OACs and patients with CHA$_2$DS$_2$-VASc score $= 0$ if male or $\leq 1$ if female not receiving OACs were considered A adherent.

The B criterion is defined as better symptom management with patient-centered and symptom-directed decisions on rate or rhythm control. In our analysis, patients were qualified for the B criterion if they had actual symptoms control. It was defined as an European Heart Rhythm Association score of I or II (no symptoms or mild symptoms) at the baseline visit.

The C criterion was defined as comorbidity and cardiovascular risk factor management. We qualified patients for the C criterion if they were treated with disease-specific treatment(s) according to current guidelines (or no management in case of no comorbidities) at the baseline visit. In the present analysis, we considered as guideline-adherent the following: 1) angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB), calcium-channel inhibitors, diuretics, or beta-blockers for hypertension; 2) ACE inhibitors or ARBs, beta-blockers, and statins for coronary artery disease; 3) statins for peripheral artery disease; 4) statins for previous ischemic stroke; 5) ACE inhibitors or ARBs and beta-blockers for heart failure; 5) insulin or oral antidiabetics for diabetes mellitus; and 6) statins for lipid disorders.

Patients were considered ABC adherent when qualified for all 3 criteria (A + B + C). Bleeding events were categorized according to the International Society on Thrombosis and Haemostasis definition. For this analysis, we included patients with available
data to evaluate the ABC criteria and available data on the 1-year follow-up. Patients ≥85 years of age were defined as extreme elderly.20

The primary objectives of this study were as follows: 1) to describe patients’ characteristics and the incidence of adverse events at 1-year follow-up of a contemporary real-world Chinese population managed with the ABC pathway, as compared with ABC-nonadherent patients; and 2) to evaluate the impact of ABC pathway-adherent management on the composite endpoint of all-cause death and any TE event (stroke, transient ischemic attack, peripheral embolism). As a secondary endpoint, we evaluated the potential effect of an ABC-adherent management on all-cause death, TE events, and major bleedings. Results were expressed as OR, 95% CI, and P value. Statistically significant variables at the univariate analysis were used to build a multivariate regression model. Of note, 5 (33.3%) of 15 variables included in the univariate analysis had missing values. The amount of missing data were 1.8% for coronary artery disease, 1.9% for sleep apnea, 0.4% for intracranial bleeding, 0.4% for extracranial bleeding, and 1.0% for first diagnosed AF. All missing values were replaced using multiple imputation (logistic regression model), and 5 imputed datasets were generated. In all analyses, a P value < 0.05 was considered statistically significant.

**Statistical Analysis.** Categorical variables are expressed as counts and percentages and continuous variables as mean ± SD. Between-group comparisons were made using a chi-square test for categorical variables and Student's t test for continuous variables. A logistic univariate regression analysis was performed to evaluate the variables potentially associated with the composite endpoint (all-cause death or any TE event), all-cause death, TE events, and major bleedings.
Statistical analysis was performed using SPSS version 24 (IBM Corp).

RESULTS

Of the 7,077 patients enrolled in the ChioTEAF registry, 6,420 (90.7%) completed the 1-year follow-up, and 3,520 (49.7%) of them had complete data to evaluate the ABC pathway (Supplemental Figure 1). Among these patients, 15 (0.4%) patients fulfilled no ABC criteria, 340 (9.7%) fulfilled 1 ABC criterion, 1,717 (48.8%) fulfilled 2 ABC criteria, and 1,448 (41.1%) fulfilled all 3 ABC criteria (Central Illustration). A total of 1,523 (43.3%) patients were female, mean age was 73.1 ± 10.4 years, and 492 (14.0%) patients were extremely elderly (Table 1).

Of note, patients not included in the present analysis were older (76.7 ± 10.6 years of age vs 73.1 ± 10.4 years of age; \( P < 0.001 \)) and had higher mean CHA\textsubscript{2}-D\textsubscript{S\textsubscript{2}}-VASc (3.83 ± 1.78 vs 3.48 ± 1.70; \( P < 0.001 \)) and HAS-BLED (2.29 ± 1.10 vs 2.10 ± 1.10; \( P < 0.001 \)) scores.

Patients managed as ABC pathway adherent were younger with similar CHA\textsubscript{2}-D\textsubscript{S\textsubscript{2}}-VASc and lower HAS-BLED scores (71.7 ± 10.3 years of age vs 74.1 ± 10.4 years of age; \( P < 0.001 \); 3.54 ± 1.60 years of age vs 3.44 ± 1.70 years of age; \( P = 0.098 \); and 1.95 ± 1.10 vs 2.12 ± 1.20; \( P < 0.001 \), respectively) compared with ABC-nonadherent patients. As expected, OACs were more often prescribed in the former group (97.2% vs 20.4%; \( P < 0.001 \)), while antiplatelets among ABC-nonadherent patients (17.4% vs 54.4%; \( P < 0.001 \)). A detailed description of the baseline characteristics for both groups is reported in Table 1.

OUTCOMES. At 1-year follow-up, patients adherent to the ABC pathway had a lower incidence of the primary composite outcome of all-cause death or any TE event (1.5% vs 3.6% per year; \( P < 0.001 \)) as compared with those nonadherent to the ABC pathway, as well as a lower incidence of all-cause death (1.0% vs 2.5% per year; \( P < 0.001 \)) and TE events (0.6% vs 1.2%, \( P = 0.047 \)). Major bleeding rate was similar (0.9% vs 0.8% per year; \( P = 0.813 \)) (Table 2).

On multivariate analysis, ABC pathway-adherent care was independently associated with a lower risk of the primary composite endpoint of all-cause death/any TE event (OR: 0.508; 95% CI: 0.306-0.843) (Table 3). Other independent predictors of the primary composite endpoint were as follows: age (OR: 1.086; 95% CI: 1.056-1.117), diabetes mellitus (OR: 1.804; 95% CI: 1.167-2.790), and heart failure (OR: 3.742; 95% CI: 2.288-6.120) (Table 3).

Benefits of the ABC pathway-adherent care were sustained in extremely elderly patients (≥85 years of age). In this subset of patients, ABC pathway...
adherence was lower than among the younger population (43.1% vs 28.9%; \( P < 0.001 \)) but was independently associated with a greater reduction in the risk of the primary composite endpoint (OR: 0.195; 95% CI: 0.067-0.565) (Supplemental Table 1). Fewer adverse events were observed across younger age strata. ABC pathway adherent care was significantly associated with a reduction in the composite endpoint especially in patients \( \geq 75 \) years of age, while it was relatively less effective in younger age strata (Supplemental Table 2).

The reduction in the composite outcome was found only if 3 ABC pathway criteria were fulfilled (Table 4). Individual adverse events per number of ABC criteria fulfilled are reported in Supplemental Table 3. Regarding the secondary endpoints, ABC pathway adherent care was associated with a reduction of all-cause death on the univariate analysis (OR: 0.387; 95% CI: 0.213-0.702), but the statistical significance was not maintained on multivariate analysis (Supplemental Table 4). On univariate analysis, TE events and major bleedings did not differ significantly between the ABC pathway-adherent and ABC pathway-nonadherent groups (OR: 0.453; 95% CI: 0.204-1.008; and OR: 1.092; 95% CI: 0.529-2.254, respectively).

**DISCUSSION**

To our knowledge, we provide one of the first insights on the impact of an integrated and holistic approach to AF management in a contemporary, real-world Chinese cohort. Our principal findings are as follows: 1) only 41.1% of patients are managed with an integrated, ABC pathway approach to holistic care; 2) the incidence of the composite endpoint (all-cause death/any TE event), all-cause death, and TE events at 1-year follow-up was significantly lower in ABC-adherent patients than in ABC-nonadherent patients, while major bleeding incidence was comparable; and 3) ABC-adherent management was an independent predictor of lower risk of the primary composite endpoint (Central Illustration), even among extreme elderly patients.

**TABLE 2** Adverse Events at 1-Year Follow-Up

|                      | ABC Adherent (n = 1,448) | ABC Nonadherent (n = 2,072) | P Value |
|----------------------|--------------------------|----------------------------|---------|
| Death/any TE event   | 21 (1.5)                 | 74 (3.6)                   | <0.001  |
| Death                | 14 (1.0)                 | 51 (2.5)                   | 0.001   |
| Any TE event         | 8 (0.6)                  | 25 (1.2)                   | 0.047   |
| Major bleeding       | 13 (0.9)                 | 17 (0.8)                   | 0.813   |

ABC = Atrial Fibrillation Better pathway; TE = thromboembolism.

**TABLE 3** Univariate and Multivariate Regression Analysis for the Composite Outcome of All-Cause Death or Any Thromboembolic Event

|                      | Univariate | Multivariate |
|----------------------|------------|--------------|
|                      | OR         | 95% CI       | P Value | OR         | 95% CI       | P Value |
| ABC adherence        | 0.398      | 0.244-0.648  | <0.001  | 0.508      | 0.306-0.843  | 0.009   |
| Age                  | 1.122      | 1.093-1.153  | <0.001  | 1.086      | 1.056-1.117  | <0.001  |
| Female               | 0.759      | 0.498-1.158  | 0.201   |            |              |         |
| First diagnosed AF   | 1.082      | 0.635-1.843  | 0.772   |            |              |         |
| Diabetes             | 2.084      | 1.377-3.154  | 0.001   | 1.804      | 1.167-2.790  | 0.008   |
| Hypertension         | 1.208      | 0.779-1.872  | 0.398   |            |              |         |
| Heart failure        | 5.937      | 3.718-9.483  | <0.001  | 3.742      | 2.288-6.120  | <0.001  |
| Coronary artery disease | 3.201    | 1.981-5.173  | <0.001  |            |              |         |
| Ischemic stroke      | 2.459      | 1.621-3.730  | <0.001  |            |              |         |
| Chronic kidney disease | 2.831     | 1.720-4.661  | <0.001  |            |              |         |
| COPD                 | 3.870      | 2.341-6.396  | <0.001  |            |              |         |
| Sleep apnea          | 1.568      | 0.622-3.957  | 0.340   |            |              |         |
| Dementia             | 4.538      | 2.016-10.218 | <0.001  |            |              |         |
| Intracranial bleeding | 3.660     | 1.427-9.389  | 0.007   |            |              |         |
| Extracranial bleeding | 1.260     | 0.455-3.489  | 0.656   |            |              |         |

Abbreviations as in Table 1.
AF is associated with an excess mortality, stroke, dementia, heart failure, depression, impaired quality of life, and hospitalizations. Moreover, AF patients are burdened by several risk factors and comorbidities. The complexity of these patients suggests that a multidisciplinary approach to patients' care may lead to better outcomes than a single disease management strategy. Indeed, a meta-analysis on 1,383 patients across 3 studies showed that an integrated care approach to care delivery was associated with a significant reduction in all-cause mortality (OR: 0.51; 95% CI: 0.32-0.80) and cardiovascular hospitalizations (OR: 0.58; 95% CI: 0.44-0.77). The ABC pathway was subsequently proposed to streamline the individual components of the integrated care approach into a simple and effective tool guiding clinicians in step-by-step decision making for holistic AF patients' management.

Our study integrates and confirms the benefit of an ABC pathway-adherent management on clinical outcomes in different AF patients’ populations, showing a 48% reduction in the risk of the composite outcome of all-cause death or any TE event. Moreover, benefits were greater among the extreme elderly, suggesting that a holistic and integrated approach to care is worth implementing among this subset of patients. Similar results were not observed in young age strata, possibly because the relatively low number of adverse events limited the statistical power of the study. In a report from the European Society of Cardiology EORP-AF General Long-Term Registry, Proietti et al reported a 41% reduction in the composite endpoint of TE events, acute coronary syndromes, or cardiovascular death; 48% reduction in cardiovascular death; and 43% decrease in all-cause death in ABC pathway-adherent patients as compared with nonadherent patients at 1-year follow-up, from a large European cohort of 6,646 patients. Similarly, Yoon et al analyzed nationwide Korean national administrative data of 204,842 patients followed for 6.2 ± 3.5 years and showed that ABC-adherent patients had a significantly lower risk of all-cause death (HR: 0.82; 95% CI: 0.78-0.86) and the composite outcome of death, ischemic stroke, major bleeding, or myocardial infarction (HR: 0.86; 95% CI: 0.83-0.89). The ABC pathway has also been tested in a prospective cluster randomized trial (mAFA-II trial), which showed a significant reduction in the rates of the composite outcome of TE events, death, or rehospitalization in patients randomized to receive integrated care based on a mobile AF application incorporating the ABC pathway, as compared with the usual-care group (1.9% vs 6.0%). In the long-term extension cohort, the benefits on clinical outcomes were maintained, and there was good adherence (>70%) and persistence (>90%) of use of the mobile health approach to implement the ABC pathway.

In our analysis, ABC pathway-adherent care was independently associated with a lower risk of the composite outcome of all-cause death or any TE event but was not an independent predictor of the individual outcomes of all-cause death, TE events, and major bleedings, although some trends were observed. These results may reflect the small sample size, the low rate of adverse events, and the relatively short follow-up, which may limit the statistical power of our study for the identification of differences in individual outcomes. Our study shows that qualifying for 3 ABC pathway criteria was independently associated with a reduction in all-cause death or any TE event. However, an increasing number of fulfilled ABC criteria was associated with a trend toward a progressively lower OR of adverse outcomes. These results highlight that all the individual components included in the ABC pathway approach would act synergistically, and a holistic approach to AF management is best to improve patients' outcomes.
The importance of a tailored, holistic treatment strategy based on individual risk assessment and patient preferences has been emphasized by the new 2020 European Society of Cardiology guidelines for the diagnosis and management of AF. A recent systematic review and meta-analysis showed that adherence to the ABC pathway is low, being adopted in only 21% of patients, but ABC pathway compliance was associated with a lower risk of all-cause death (OR: 0.42; 95% CI: 0.31-0.56), cardiovascular death (OR: 0.37; 95% CI: 0.23-0.58), stroke (OR: 0.55; 95% CI: 0.37-0.82), and major bleeding (OR: 0.69; 95% CI: 0.51-0.94).

The prevalence of ABC-adherent patients in our cohort was higher (approximately 40%) but still suboptimal, suggesting that further efforts should be made to implement this effective strategy in everyday clinical practice. To achieve this goal, engagement with patients and health care professionals is crucial, and the simplicity of the ABC pathway represents a major strength to guide patients’ understanding of their management plan and physicians’ decision making.

**STUDY LIMITATIONS.** The observational nature of this registry may limit the generalizability of the results and the power to detect differences in individual outcomes. As in the majority of real-life observational registries, clinical outcomes were not centrally adjudicated and may be over- or underestimated. This survey was conducted before the publication of the current AF guidelines implementing the ABC pathway into AF care, and the enrollment period was relatively long, which implies a potential variability in the therapeutic strategies for AF management. Therefore, a residual bias arising from differences in patients’ follow-up management or risk profile cannot be completely ruled out. The multivariate analysis, adjusted for a large set of covariates, shows an independent association between ABC-adherent management and improvement in clinical outcomes. Data on anti-coagulation control, management of cardiovascular risk factors (eg, obesity, smoking), or patient’s drug contraindications are not available and may not be considered in this analysis. Because only 49.7% of the overall cohort was included in the present analysis, selection bias cannot be completely ruled out. As previously described, patients not included were older and had higher mean CHA2DS2-VASc and HAS-BLED scores. The ChiOTEAF registry aim was to analyze the relationship between the general management of AF and cardiovascular events at 6 months and 12 months and was not specifically designed to determine the role of ABC pathway-adherent care on patients’ prognosis. The retrospective nature of our analysis limits the strength of the association between an ABC pathway-adherent care and better clinical outcomes. The prospective implementation of the ABC pathway has been already tested in the mAFA-II trial as well as ongoing prospective studies that are specifically designed and adequately powered. Finally, we acknowledge that the effects of other interventions on modifiable cardiovascular risk factors that require continuous patients’ education, such as lifestyle changes, alcohol reduction, and treatment of obstructive sleep apnea with continuous positive airway pressure were not assessed.

**CONCLUSIONS**

In a contemporary nationwide cohort of Chinese AF patients, adherence to the ABC pathway for integrated care was suboptimal, but clinical management adherent to the ABC pathway was associated with better outcomes. Further efforts to implement this effective holistic AF management strategy in everyday clinical practice would improve patient outcomes.

**ACKNOWLEDGMENTS** The authors thank all the participants into the ChiOTEAF registry for their contributions. ChiOTEAF registry investigators are listed in the Supplemental Appendix.

**FUNDING SUPPORT AND AUTHOR DISCLOSURES**

This study was supported by Beijing Natural Science Foundation (2141100002114050) and Chinese Military Health Care (J17B1508). Dr Lip has served as a consultant and speaker for Bristol-Myers Squibb/Pfizer, Boehringer Ingelheim, and Daiichi Sankyo (no fees received personally). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

**ADDRESS FOR CORRESPONDENCE:** Dr Gregory Y.H. Lip, Liverpool Centre for Cardiovascular Science, Institute of Life Course & Medical Sciences, William Henry Duncan Building, 6 West Derby Street, Liverpool L7 8TX, United Kingdom. E-mail: gregory.lip@liverpool.ac.uk. OR Dr Yutang Wang, Department of Cardiology, Second Medical Centre, Chinese PLA General Hospital, 28 Fuxing Road, Beijing 100853, China. E-mail: wyt301@yeah.net.
ABC Pathway Adherent Care Improves Outcomes in Atrial Fibrillation

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: The ABC pathway has been proposed to streamline the integrated and holistic approach to AF care. Clinical management adherent to the ABC pathway was associated with better outcomes in a contemporary Chinese cohort of patients with AF.

TRANSLATIONAL OUTLOOK: Adherence to the ABC pathway for integrated care should improve. Further studies are needed to address potentially actionable clinical and organizational obstacles to ABC pathway implementation.

REFERENCES

1. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med. 2007;146(12):857-867.
2. Lane DA, Lip GYH. Stroke and bleeding risk stratification in atrial fibrillation: a critical appraisal. Eur Heart J Suppl. 2020;22(Suppl O):014-O27.
3. Kotalczyk A, Mazurek M, Kalarus Z, Potpara TS, Lip GYH. Stroke prevention strategies in high-risk patients with atrial fibrillation. Nat Rev Cardiol. 2021;18(4):276-290.
4. Odutayo A, Wong CX, Hsiao AJ, Hopewell S, Altman DG, Emdin CA. Atrial fibrillation and risks of cardiovascular disease, renal disease, and death: systematic review and meta-analysis. BMJ. 2016;354:i4482.
5. Kwok CS, Liske YK, Hale R, Potter JF, Myint PK. Atrial fibrillation and incidence of dementia: a systematic review and meta-analysis. Neurology. 2011;76(10):914-922.
6. Polakony SD, Piccini JP, Stevens SR, et al. Cause of death and predictors of all-cause mortality in anticoagulated patients with nonvalvular atrial fibrillation: data from ROCKET AF. J Am Heart Assoc. 2016;5(3):e002197.
7. Fauchier L, Leocq C, Clementy N, et al. Oral anticoagulation and the risk of stroke or death in patients with atrial fibrillation and an additional stroke risk factor: The Loire Valley Atrial Fibrillation Project. Chest. 2016;149(4):960-968.
8. Potpara TS, Lip GYH, Blomstrom-Lundqvist C, et al. The 4S-AF scheme (stroke risk; symptoms; severity of burden; substrate): a novel approach to in-depth characterization (rather than classification) of atrial fibrillation. Thromb Haemost. 2021;121(3):270-278.
9. Gallagher C, Elliott AD, Wong CX, et al. Integrated care in atrial fibrillation: a systematic review and meta-analysis. Heart. 2017;103(24):1947-1953.
10. Lip GYH. The ABC pathway: an integrated approach to improve AF management. Nat Rev Cardiol. 2017;14(11):627-628.
11. Proietti M, Romiti GF, Olshansky B, Lane DA, Lip GYH. Improved outcomes by integrated care of anticoagulated patients with atrial fibrillation using the simple ABC (Atrial Fibrillation Better Care) pathway. Am J Med. 2018;131(11):1359-1366.e6.
12. Pastori D, Pignatelli P, Menichelli D, Violi F, Lip GYH. Integrated care management of patients with atrial fibrillation and risk of cardiovascular events: the ABC (Atrial fibrillation Better Care) pathway in the ATHERO-AF study cohort. Mayo Clin Proc. 2019;94(7):1261-1267.
13. Yoon M, Yang PS, Jang E, et al. Improved population-based clinical outcomes of patients with atrial fibrillation with compliance with the simple ABC (Atrial Fibrillation Better Care) pathway for integrated care management: a nationwide cohort study. Thromb Haemost. 2019;121(10):1695-1703.
14. Proietti M, Lip GYH, Laroche C, et al. Relation of outcomes to ABC (Atrial Fibrillation Better Care) pathway adherent care in European patients with atrial fibrillation: an analysis from the ESC-EHRA EORP Atrial Fibrillation General Long-Term (AFGen LT) Registry. Europace. 2021;23(2):174-183.
15. Gao Y, Wang Y, Li X, et al. Optimal Thrombo- prophylaxis in Elderly Chinese Patients with Atrial Fibrillation (ChiOTeAF) registry: protocol for a prospective, observational nationwide cohort study. BMJ Open. 2018;8(5):e020191.
16. Lip GY, Laroche C, Dan GA, et al. A prospective survey in European Society of Cardiology member countries of atrial fibrillation management: baseline results of EUObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry. Europace. 2014;16(3):308-319.
17. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crinjs HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest. 2010;137(2):263-272.
18. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crinjs HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest. 2010;138(5):1093-1100.
19. Schulman S, Kearon C. Subcommittee on Control of Anticoagulation of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis. Definition of major bleeding in clinical investigations of antithrombotic medicinal products in non-surgical patients. J Thromb Haemost. 2005;3(4):692-694.
20. Yamashita Y, Hamatani Y, Esato M, et al. Clinical characteristics and outcomes in extreme elderly (age ≥ 85 years) Japanese patients with atrial fibrillation: the Fushimi AF registry. Chest. 2016;149(2):401-412.
21. Kim MH, Johnston SS, Chu BC, Dalal MR, Schulman KL. Estimation of total incremental health care costs in patients with atrial fibrillation in the United States. Circ Cardiovasc Qual Outcomes. 2011;4(3):313-320.
22. Freeman JV, Simon DN, Go AS, et al. Association between atrial fibrillation symptoms, quality of life, and patient outcomes: results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). Circ Cardiovasc Qual Outcomes. 2015;8(4):393-402.
23. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991;22(8):983-988.
24. Proietti M, Marzona I, Vannini T, et al. Long-Term relationship between atrial fibrillation, multimorbidity and oral anticoagulant drug use. Mayo Clin Proc. 2019;94(12):2427-2436.
25. Guo Y, Lane DA, Wang L, et al. Mobile health technology to improve care for patients with atrial fibrillation. J Am Coll Cardiol. 2020;75(13):1523-1534.
26. Guo Y, Guo J, Shi X, et al. Mobile health technology-supported atrial fibrillation screening and integrated care: a report from the mAFA-II trial. Long-term Extension Cohort. Eur J Intern Med. 2020;82:105-111.
27. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2021;42(3):373-498.
28. Romiti GF, Pastori D, Rivera-Caravaca JM, et al. Adherence to the ‘Atrial Fibrillation Better Care’ (ABC) pathway in patients with atrial fibrillation. Thromb Haemost. 2022;122(03):406-414.

APPENDIX For expanded Methods and Results sections as well as supplemental tables and a figure, please see the online version of this paper.