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ORIGINAL RESEARCH

Effects of the Atrial Fibrillation Better Care Pathway on Outcomes Among Clinically Complex Chinese Patients With Atrial Fibrillation With Multimorbidity and Polypharmacy: A Report From the ChiOTEAF Registry

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BACKGROUND: Patients with atrial fibrillation commonly have complex clinical backgrounds of multimorbidity and polypharmacy. The Atrial Fibrillation Better Care (ABC) pathway has been developed to help deliver integrated and holistic care for patients with atrial fibrillation. In this ancillary analysis, we assessed the adherence to and the effectiveness of the ABC pathway at reducing adverse outcomes in Chinese patients with atrial fibrillation with a complex clinical background of multimorbidity or polypharmacy.

METHODS AND RESULTS: The ChiOTEAF (Optimal Thromboprophylaxis in Elderly Chinese Patients With Atrial Fibrillation) registry is a prospective, multicenter, nationwide study conducted from October 2014 to December 2018. The primary outcomes of interest were the composite end point of all-cause death and thromboembolic events, as well as individual end points of all-cause death, thromboembolic events, and major bleeding. *Multimorbidity* was defined as the presence of ≥2 comorbidities, and *polypharmacy* was defined as the concomitant use of ≥5 medications. The eligible cohort included 4644 patients with multimorbidity, of whom 2610 (56.2%) had available data to assess the ABC pathway usage (mean age, 74.4±10.2; 42.8% women). Among patients with polypharmacy (n=2262; mean age, 74.6±10.1; 43.3% women), 1328 (58.7%) had available data to assess the use of the ABC pathway. Adherence to the ABC pathway was associated with a lower risk of the primary composite outcome among patients with multimorbidity (odds ratio, 0.48; 95% CI, 0.29–0.79) and in the polypharmacy group (odds ratio, 0.39; 95% CI, 0.19–0.78). Health-related quality of life was lower in the non–ABC-adherent group compared with the ABC-treated patients.

CONCLUSIONS: This nationwide real-world registry shows that adherence to the ABC pathway is associated with improved clinical outcomes and health-related quality of life in clinically complex Chinese patients with atrial fibrillation with multimorbidity or polypharmacy.

Key Words: Asia ■ atrial fibrillation ■ multimorbidity ■ polypharmacy ■ registry

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CLINICAL PERSPECTIVE

What Is New?

- Adherence to the Atrial Fibrillation Better Care pathway is associated with improved outcomes when managing clinically complex Chinese patients with multimorbidity or polypharmacy.

What Are the Clinical Implications?

- Patients with multimorbidity or polypharmacy are considered challenging to manage when associated with atrial fibrillation.
- Use of the Atrial Fibrillation Better Care pathway is feasible among these patients and improves clinical outcomes and health-related quality of life.
- This may lead to lower health care costs and mortality rates.

Nonstandard Abbreviations and Acronyms

ABC	Atrial Fibrillation Better Care
ChiOTEAF	Optimal Thromboprophylaxis in Elderly Chinese Patients with Atrial Fibrillation
OAC	oral anticoagulant

The importance and evident benefits of a well-rounded holistic and integrated approach to evaluation, characterization, and management of atrial fibrillation (AF) have been emphasized in recent guidelines.[1–3] Standardizing holistic management through protocolization and implementation of framework models can lead to improved patient care.[4,5] The Atrial Fibrillation Better Care (ABC) pathway promotes such an integrated approach to AF management[6]: (A) avoid stroke; (B) better symptom control, with patient-centered symptom-guided decisions on rate or rhythm control; and (C) cardiovascular risk factor and comorbidity optimization, including lifestyle changes.[7] The ABC pathway offers a systematic approach to AF management that has been shown to be associated with improved clinical outcomes and significantly lower health-related costs in retrospective and prospective cohorts as well as a prospective randomized trial (mAFA [Mobile Atrial Fibrillation Application]-II), even in subgroups of clinically complex patients.[8–12]

Patients with AF often have multiple comorbidities,[13,14] which consequently lead to polypharmacy,[15–17] frequent hospital admissions,[18] higher health care costs,[19] and higher mortality rates.[15,20–25] These patients are considered challenging to manage in both the community and hospital settings because of such a complex clinical background commonly being associated with AF.

In this ancillary analysis of the contemporary nationwide registry, we assessed the adherence to and the effectiveness of the ABC pathway at reducing the adverse outcomes in Chinese patients with AF with a complex clinical background of multimorbidity or polypharmacy.

METHODS

Ethics Approval

This study was performed in line with the principles of the Declaration of Helsinki. Ethics approval was granted by the Central Medical Ethic Committee of Chinese PLA General Hospital (approval No. S2014-065-01).

Consent to Participate

Written informed consent was obtained from all individual participants included in the study. Consent for publication was not applicable. Authors are responsible for correctness of the statements provided in the article.

Data Availability Statement

The data sets used and analyzed during the current study are available from the corresponding author on reasonable request.

The ChiOTEAF (Optimal Thromboprophylaxis in Elderly Chinese Patients With Atrial Fibrillation) is a prospective cohort study. The protocol of the ChioTEAF registry, the method of implementation of the ABC pathway, and the characteristics of patients with multimorbidity and polypharmacy have been previously described.[26–28] The study was conducted between October 2014 and December 2018 at 44 sites in 20 Chinese provinces. The study enrolled consecutive patients with AF (with a documented AF episode within 12 months before enrollment) presenting to cardiology, neurology, or surgical services. Follow-up visits were performed at 6 and 12 months and thereafter annually for the next 2 years. Data were gathered by the local investigators at the point of enrollment and during follow-up visits (face-to-face follow-up and/or telephone follow-up and/or chart review).

Multimorbidity was defined as the presence of ≥2 comorbidities (in addition to AF) at enrollment.[29,30] *Polypharmacy* was defined as the concomitant use of ≥5 medications (regardless of the reasons and utility) at enrollment.[31]

The participants were assessed against the ABC pathway criteria according to its original definition: patients qualified for the "A" criterion if they were treated

with oral anticoagulants (OACs) according to their thromboembolic risk; the "B" criterion if they demonstrated optimal symptom control defined as European Heart Rhythm Association score of I (no symptoms) or II (mild symptoms) at baseline; "C" criterion if they received disease-specific treatment(s) according to current guidelines at baseline. Patients were considered as ABC adherent if they fulfilled all 3 criteria (A+B+C).

Other variables were defined in line with the EORP-AF (EURObservational Research Programme Atrial Fibrillation) long-term general registry[32] protocol. The CHA_2DS_2-VASc score[33] and the HAS-BLED bleeding score[34] were used to assess the thromboembolic and bleeding risks. Bleeding events (intracranial and extracranial haemorrhages) were categorized on the basis of the International Society on Thrombosis and Haemostasis definition.[35] The EuroQol 5 dimensions questionnaire (EQ-5D-5L)[36] was used to assess the patient-reported quality of life.

Objectives

The primary objective of the present analysis was to evaluate the impact of ABC pathway adherence on the clinical outcomes among patients with multimorbidity and patients with polypharmacy at 1 year of follow-up. The primary outcomes of interest were the composite end point of all-cause death and thromboembolic events (ischemic stroke, transient ischemic attack, or peripheral embolism), as well as individual end points of all-cause death, thromboembolic events, and major bleeding. The secondary objectives included (1) identifying the potential predictors of the compliance with the ABC pathway among multimorbid patients with AF; (2) evaluating the impact of the ABC pathway on clinical outcomes among the subgroup of patients with concomitant multimorbidity and polypharmacy; and (3) evaluating the impact of the ABC pathway on clinical outcomes among the overall multimorbidity and polypharmacy cohorts, that is, comparing ABC-adherent patients with multimorbidity or polypharmacy with all other patients with multimorbidity or polypharmacy, respectively, regardless of the availability of the ABC pathway usage data.

Statistical Analysis

Continuous variables were reported as mean± SD; between-group comparisons were made using Student's *t* test or the Mann-Whitney *U* test (based on distribution). Categorical variables were reported as counts and percentages; between-group comparisons were made by the χ^2 test. The quality of life was assessed on the basis of the EuroQol summary index (range, 0–1; a score of 1 indicating the best health state) estimated from the EuroQol 5 dimensions questionnaire value set for China.[37] Logistic regression analysis was performed to assess the age-adjusted associations between the ABC compliance and clinical outcomes (composite outcome of all-cause death/any thromboembolic, all-cause death, thromboembolic events, and major bleeding) among patients with AF with (1) multimorbidity and (2) polypharmacy. For the secondary objectives, a logistic univariate regression analysis was used to identify the predictors of ABC compliance in the multimorbidity group. All the significant variables were included in a multivariate regression model. Finally, sensitivity analysis was performed for (1) patients with AF with both multimorbidity and polypharmacy, (2) the overall multimorbidity cohort, and (3) the overall polypharmacy cohort. Results were expressed as odds ratio (OR) with 95% CI. In all analyses, a *P* value <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 24 (IBM Corp., Armonk, NY).

RESULTS

The ChiOTEAF registry enrolled 7077 patients, of whom 657 (9.3%) were lost to follow-up at 1 year (Figure 1). Among patients with multimorbidity (n=4644), 2610 (56.2%) had available data to assess ABC pathway usage (mean age, 74.4±10.2; 42.8% women). Among patients with polypharmacy (n=2262), 1328 (58.7%) had available data to assess the use of the ABC pathway (mean age, 74.6±10.1; 43.3% women).

Multimorbidity Subgroup

Of the multimorbidity cohort, 1133 of 2610 (43.4%) patients were managed in accordance with the ABC pathway. Multimorbid patients with AF treated according to the ABC pathway were younger (mean age, 72.8±10.1 versus 75.7±10.1; *P*<0.001), with a lower proportion of patients with a first diagnosis of AF (13.7% versus 19.8%; *P*<0.001), coronary artery disease (54.9% versus 67.6%; *P*<0.001), and heart failure (39.6% versus 44.4%; *P*=0.014), compared with the non-ABC group. Antiplatelet agents were used in 63.8% and OACs in 11.6% of patients in the non-ABC group. Health-related quality of life was lower in the non–ABC-adherent group (mean EuroQol, 0.81±0.19 versus 0.84±0.17; *P*<0.001) compared with the ABC-managed patients. Baseline characteristics are reported in Table 1.

Clinical Outcomes

Among multimorbid patients with AF managed according to the ABC pathway, a lower incidence of the composite outcome (1.8% versus 4.7%; *P*<0.001), all-cause death (1.1% versus 3.2%; *P*=0.001), and thromboembolic events (0.7% versus 1.6%; *P*=0.034) was observed compared with the non-ABC group. ORs of the composite outcome (0.48; 95% CI, 0.29–0.79) and

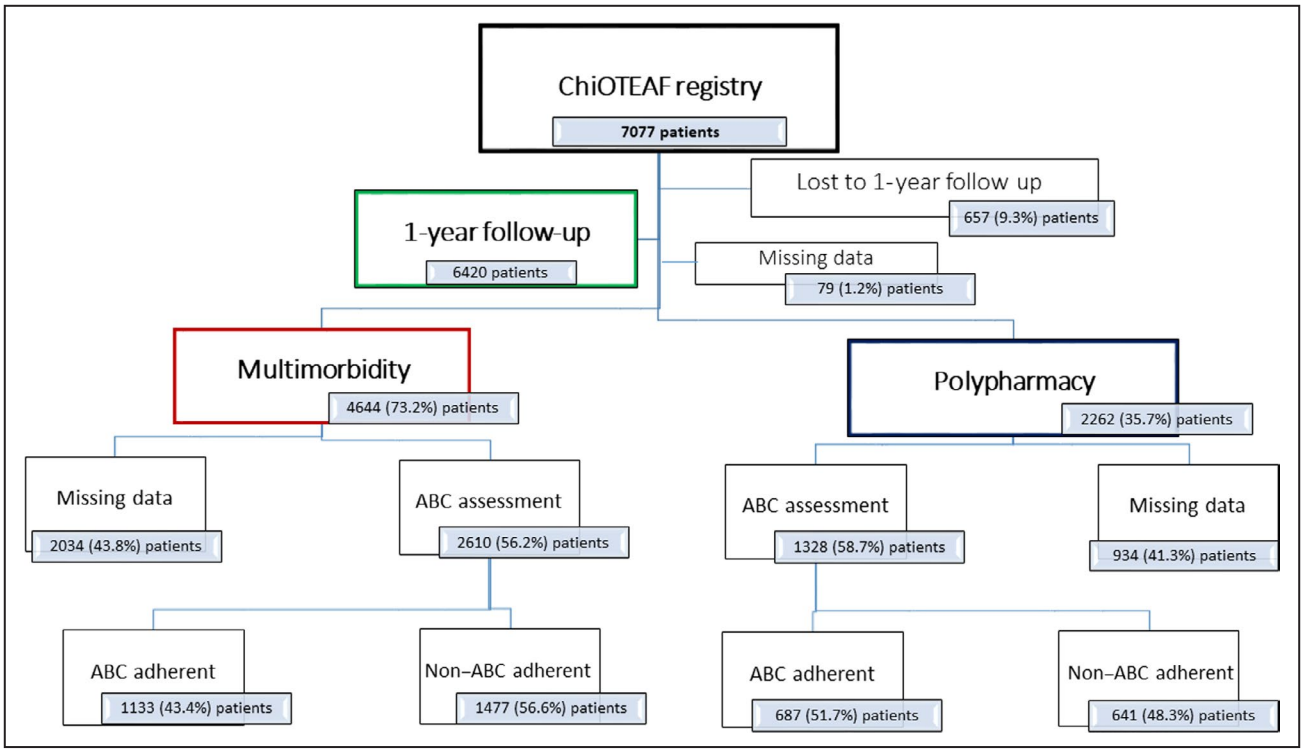

Figure 1. Flowchart of patient inclusion.
ABC indicates Atrial Fibrillation Better Care; and ChiOTEAF, Optimal Thromboprophylaxis in Elderly Chinese Patients With Atrial Fibrillation.

all-cause death (0.51; 95% CI, 0.27–0.95) were lower in the ABC-managed patients. No statistically significant differences were reported in major bleeding between the groups (Table 2).

Predictors of ABC Compliance

A multivariate analysis showed that (1) older age (OR, 0.98; 95% CI, 0.97–0.99), coronary artery disease (OR, 0.55; 95% CI, 0.46–0.65), prior major bleeding (OR, 0.14; 95% CI, 0.06–0.29), chronic kidney disease (OR, 0.66; 95% CI, 0.51–0.86), and chronic obstructive pulmonary disease (OR, 0.71; 95% CI, 0.53–0.96) were the independent predictors of poor compliance with the ABC pathway; while (2) hypertension (OR, 1.50; 95% CI, 1.23–1.82) and polypharmacy (OR, 2.15; 95% CI, 1.81–2.55) were associated with a better adherence to the ABC pathway among the patients with multimorbidity (Figure 2; Table S1).

Polypharmacy Subgroup

Among patients with polypharmacy 687 of 1328 (51.7%) were managed according to the ABC pathway. Baseline characteristics are reported in Table 1.

Patients in the ABC group were younger (mean age, 72.9±10.1 versus 76.5±9.7; *P*<0.001), with a higher proportion of patients with hypertension (79.2% versus 74.6%; *P*=0.046), and lower HAS-BLED score (2.2±1.0 versus 2.6±1.1; *P*<0.001) compared with the non-ABC group. As expected, differences in the use of OACs were evident between groups, including direct OACs to be favored over vitamin K antagonists (53.6% versus 46.3%) in the ABC group; antiplatelet agents were used in 87.5% and OACs in 8.4% of patients in the non-ABC group. The use of the rhythm control strategies including amiodarone (28.4% versus 16.2; *P*<0.001) and AF ablation (18.2% versus 3.9%; *P*<0.001) were more prevalent in the ABC-adherent group. Health-related quality of life was lower in the non–ABC-adherent group (mean EuroQol, 0.83±0.18 versus 0.80±0.20; *P*=0.017) compared with the ABC-managed patients.

Clinical Outcomes

Among the patients with AF with polypharmacy managed according to the ABC pathway, a lower incidence of the composite outcome (1.6% versus 5.1%; *P*<0.001), all-cause death (1.2% versus 3.1%; *P*=0.013), and thromboembolic events (0.6% versus 2.3%; *P*=0.007) was observed compared with the non-ABC group. ORs of the composite outcome (0.39; 95% CI, 0.19–0.78) and thromboembolic events (0.31; 95% CI, 0.10–0.95) were lower in the ABC-managed patients. No significant differences were reported in the incidence of major bleeding between groups (Table 3).

Table 1. Baseline Characteristics of the Study Cohort

	Total multimorbidity n=2610 n (%)	ABC group n=1133 n (%)	Non-ABC group n=1477 n (%)	*P* value	Total polypharmacy n=1328 n (%)	ABC group n=687 n (%)	Non-ABC group n=641 n (%)	*P* value
Age, y*	74.4±10.2	72.8±10.1	75.7±10.1	<0.001	74.6±10.1	72.9±10.1	76.5±9.7	<0.001
Female sex	1116 (42.8)	497 (43.9)	619 (41.9)	0.317	575 (43.3)	305 (44.4)	270 (42.1)	0.403
BMI, kg/m^2*	24.4±3.7	24.6±3.8	24.2±3.6	0.005	24.7±3.5	24.8±3.5	24.5±3.6	0.109
First diagnosed AF	433 (17.1)	150 (13.7)	283 (19.8)	<0.001	247 (19.1)	102 (15.2)	145 (23.3)	<0.001
Medical history								
Diabetes	879 (33.7)	386 (34.1)	493 (33.4)	0.711	530 (39.2)	267 (38.9)	253 (39.5)	0.821
Hypertension	1951 (74.8)	901 (79.5)	1050 (71.1)	<0.001	1022 (77.0)	544 (79.2)	478 (74.6)	0.046
Heart failure	1105 (42.3)	449 (39.6)	656 (44.4)	0.014	606 (45.6)	291 (42.4)	315 (49.1)	0.013
Coronary artery disease	1620 (62.1)	622 (54.9)	998 (67.6)	<0.001	870 (65.5)	399 (58.1)	471 (73.5)	<0.001
Liver disease	116 (4.4)	43 (3.8)	73 (4.9)	0.159	45 (3.4)	25 (3.6)	20 (3.1)	0.602
Lipid disorder	1617 (62.0)	757 (66.8)	869 (58.2)	<0.001	846 (63.7)	449 (65.4)	397 (61.9)	0.195
Prior ischemic stroke	766 (29.3)	346 (30.5)	420 (28.4)	0.242	367 (27.6)	197 (28.7)	170 (26.5)	0.380
Chronic kidney disease	325 (12.5)	105 (9.3)	220 (14.9)	<0.001	160 (12.0)	65 (9.5)	95 (14.8)	0.003
COPD	249 (9.5)	79 (7.0)	170 (11.5)	<0.001	113 (8.5)	48 (7.0)	65 (10.1)	0.040
Sleep apnea	114 (4.4)	55 (4.9)	59 (4.0)	0.287	57 (4.3)	34 (4.9)	23 (3.6)	0.221
Dementia	61 (2.3)	15 (1.3)	46 (3.1)	0.003	23 (1.7)	7 (1.0)	16 (2.5)	0.039
Prior major bleeding	88 (3.4)	7 (0.6)	81 (5.5)	<0.001	33 (2.5)	3 (0.4)	30 (4.7)	<0.001
CHA_2DS_2VASc*	3.9±1.6	3.9±1.6	3.9±1.6	0.743	4.1±1.6	4.0±1.6	4.1±1.7	0.142
HAS-BLED*	2.3±1.1	2.1±1.1	2.4±1.1	<0.001	2.4±1.1	2.2±1.0	2.6±1.1	<0.001
Medications								
OAC	1291 (49.5)	1119 (98.8)	172 (11.6)	<0.001	740 (55.7)	686 (99.9)	54 (8.4)	<0.001
VKA	595 (22.8)	517 (45.6)	78 (5.3)	<0.001	348 (26.2)	318 (46.3)	30 (4.7)	<0.001
DOAC	695 (26.6)	602 (53.1)	93 (6.3)	<0.001	391 (29.4)	368 (53.6)	23 (3.6)	0.010
Antiplatelet	1174 (45.0)	232 (20.5)	942 (63.8)	<0.001	761 (57.3)	200 (29.1)	561 (87.5)	<0.001
Aspirin (n=2609)	869 (33.3)	174 (15.4)	695 (47.1)	<0.001	567 (42.7)	147 (21.4)	420 (65.6)	<0.001
Clopidogrel (n=2609)	557 (21.3)	90 (7.9)	467 (31.6)	<0.001	370 (27.9)	78 (11.4)	292 (45.7)	<0.001
Ticagrelor (n=2609)	10 (0.4)	3 (0.3)	7 (0.5)	0.391	7 (0.5)	1 (0.1)	6 (0.9)	0.047
Dual antiplatelet (n=2608)	283 (10.9)	39 (3.4)	244 (16.5)	<0.001	198 (14.9)	31 (4.5)	167 (26.2)	<0.001

(*Continued*)

Table 1. (Continued)

	Total multimorbidity n=2610 n (%)	ABC group n=1133 n (%)	Non-ABC group n=1477 n (%)	*P* value	Total polypharmacy n=1328 n (%)	ABC group n=687 n (%)	Non-ABC group n=641 n (%)	*P* value
OAC+antiplatelet	245 (9.4)	220 (19.4)	25 (1.7)	<0.001	216 (16.3)	199 (29.0)	17 (2.7)	<0.001
Digoxin	279 (10.7)	117 (10.3)	162 (11.0)	0.599	242 (18.2)	114 (16.6)	128 (20.0)	0.111
β-blockers	1558 (59.7)	732 (64.6)	826 (55.9)	<0.001	1030 (77.6)	526 (76.6)	504 (78.6)	0.368
Amiodarone	439 (16.8)	249 (22.0)	190 (12.9)	<0.001	299 (22.5)	195 (28.4)	104 (16.2)	<0.001
Propafenone	122 (4.7)	50 (4.4)	72 (4.9)	0.580	59 (4.4)	31 (4.5)	28 (4.4)	0.899
ACE-I	470 (18.0)	240 (21.2)	230 (15.6)	<0.001	344 (25.9)	189 (27.5)	155 (24.2)	0.166
ARB	732 (28.0)	396 (35.0)	336 (22.7)	<0.001	541 (40.7)	301 (43.8)	240 (37.4)	0.018
Calcium channel blockers	736 (28.2)	313 (27.6)	423 (28.6)	0.569	524 (39.5)	256 (37.3)	268 (41.8)	0.090
Diuretics	838 (32.1)	350 (30.9)	488 (33.0)	0.244	634 (47.7)	292 (42.5)	342 (53.4)	<0.001
Statins	1820 (69.7)	852 (75.2)	968 (65.5)	<0.001	1123 (84.6)	574 (83.6)	549 (85.6)	0.291
Insulin	232 (8.9)	96 (8.5)	136 (9.2)	0.513	181 (13.6)	85 (12.4)	96 (15.0)	0.167
Sulfonylureas	158 (6.1)	90 (7.9)	68 (4.6)	<0.001	126 (9.5)	75 (10.9)	51 (8.0)	0.066
Biguanide	234 (9.0)	133 (11.7)	101 (6.8)	<0.001	191 (14.4)	119 (17.3)	72 (11.2)	0.002
Nitrates	798 (30.6)	305 (26.9)	493 (33.4)	<0.001	638 (48.0)	264 (38.4)	374 (58.3)	<0.001
Polypharmacy	1203 (46.1)	621 (54.8)	582 (39.4)	<0.001	…		…	…
Quality of life								
EHRA score*	1.61±0.53	1.58±0.49	1.63±0.55	0.016	1.62±0.53	1.57±0.49	1.66±0.56	0.003
EQ index*	0.83±0.18	0.84±0.17	0.81±0.19	<0.001	0.82±0.19	0.83±0.18	0.80±0.20	0.017
AF management								
OAC persistence at 12-mo (n=2559)	1119 (43.7)	854 (76.2)	265 (18.4)	<0.001	633 (48.5)	539 (79.3)	94 (15.0)	<0.001
AF ablation (n=2608)	304 (11.7)	212 (18.7)	92 (6.2)	<0.001	150 (11.3)	125 (18.2)	25 (3.9)	<0.001
CIED (n=2608)	250 (9.6)	91 (8.0)	159 (10.8)	0.019	123 (9.3)	55 (8.0)	68 (10.6)	0.100

ABC, indicates Atrial Fibrillation Better Care; ACE-I, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; BMI, body mass index; CIED, cardiac implantable electronic device; COPD, chronic obstructive pulmonary disease; DOAC, direct-acting oral anticoagulant; EHRA, European Heart Rhythm Association; EQ, EuroQoL; OAC, oral anticoagulation; and VKA, vitamin K antagonist.
*Mean±SD.

Table 2. Effects of ABC Compliance on Clinical Outcomes Among Patients With Multimorbidity

Outcomes	ABC n=1133 n (%)	Non-ABC n=1477 n (%)	*P* value*	Odds ratio† (95% CI)
Composite outcome‡	20 (1.8)	69 (4.7)	<0.001	0.48 (0.29–0.79)
All-cause death	13 (1.1)	47 (3.2)	0.001	0.51 (0.27–0.95)
Thromboembolism events	8 (0.7)	24 (1.6)	0.034	0.48 (0.22–1.09)
Major bleeding	13 (1.1)	16 (1.1)	0.885	1.28 (0.61–2.70)

ABC indicates Atrial Fibrillation Better Care.
*Between-group comparison made by χ^2 test.
†Adjusted for age.
‡Composite outcome of all-cause death/any thromboembolism.

Exploratory Analysis

A subgroup of 1203 patients had both multimorbidity and polypharmacy; among these, 621 (51.6%) were managed according to the ABC pathway. Among patients managed according to the ABC pathway, a lower incidence of the composite outcome (1.6% versus 5.3%; *P*<0.001), all-cause death (1.1% versus 3.1%; *P*=0.017), and thromboembolic events (0.6% versus 2.6%; *P*=0.007) was observed compared with the non-ABC group. ORs of the composite outcome (0.38; 95% CI, 0.18–0.79) and thromboembolic events (0.31; 95% CI, 0.10–0.94) were lower in the ABC-adherent patients. Nonsignificant differences were reported in major bleeding (Table S2).

We performed an additional analysis for patients with AF with multimorbidity managed according to the ABC pathway compared with the overall multimorbidity cohort regardless of the availability of the ABC data (Table S3). Among the ABC-adherent group, a lower incidence of the composite outcome (1.8% versus 12.6%; *P*<0.001), all-cause death (1.1% versus 10.7%; *P*<0.001), thromboembolic events (0.7% versus 2.4%; *P*<0.001), and major bleeding (1.1% versus 2.2%; *P*<0.001) was observed. The ABC pathway was associated with lower ORs for the composite outcome (0.19; 95% CI, 0.12–0.30), all-cause death (0.15; 95% CI, 0.09–0.27), and thromboembolic events (0.39; 95% CI, 0.19–0.83).

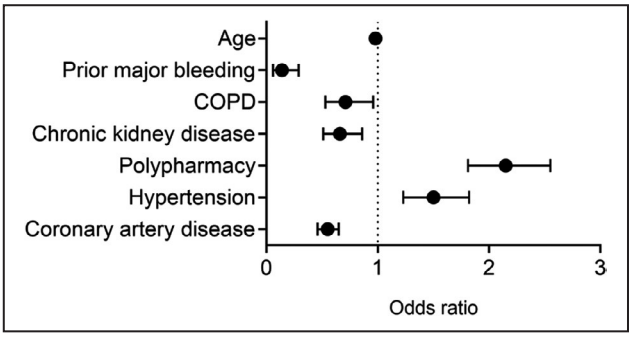

Figure 2. Predictors of the ABC compliance among patients with atrial fibrillation and multimorbidity.
ABC indicates Atrial Fibrillation Better Care; and COPD, chronic obstructive pulmonary disease.

Analogous exploratory analysis was performed for the overall polypharmacy cohort (Table S4). ABC pathway compliance was associated with lower ORs for the composite outcome (0.19; 95% CI, 0.10–0.36), all-cause death (0.18; 95% CI, 0.09–0.37), and thromboembolic events (0.35; 95% CI, 0.12–0.99) among the patients with AF with polypharmacy.

DISCUSSION

To date, the implementation of the ABC pathway and its impact on management and clinical outcomes (including health-related quality of life) among clinically complex Asian patients with AF are scarce. Herein, we demonstrate the following principal findings on the effects of usage of the ABC pathway in patients with AF with multimorbidity or polypharmacy: (1) Adherence to the ABC pathway was associated with improved clinical outcomes among complex AF patients; (2) various clinical predictors were independently associated with ABC adherence among multimorbidity patients; and (3) health-related quality of life was lower in the non–ABC-adherent group compared with the ABC-managed patients.

Our results are comparable to the results of the post hoc ancillary analysis from the AFFIRM (Atrial Fibrillation Follow-Up Investigation of Rhythm Management) trial (conducted over 2 decades ago), which showed that adherence to the ABC pathway in patients with multimorbidity, polypharmacy, and multiple hospitalizations was associated with a significantly lower cumulative risk of the composite outcome of all-cause hospitalization and all-cause death.[10] Our analysis adds to these findings by demonstrating that better clinical outcomes are observed in a contemporary cohort of Chinese patients with AF with both multimorbidity and polypharmacy who adhere to the ABC pathway.

Patients who received ABC management were more likely to be younger, less likely to have been diagnosed with AF for the first time, and have existing coronary artery disease or heart failure compared with those who did not receive ABC management.

Table 3. Effects of ABC Compliance on Clinical Outcomes Among Patients With Polypharmacy

Outcomes	ABC n=687 n (%)	Non-ABC n=641 n (%)	*P* value*	Odds ratio† (95% CI)
Composite outcome‡	11 (1.6)	33 (5.1)	<0.001	0.39 (0.19–0.78)
All-cause death	8 (1.2)	20 (3.1)	0.013	0.48 (0.21–1.12)
Thromboembolic events	4 (0.6)	15 (2.3)	0.007	0.31 (0.10–0.95)
Major bleeding	10 (1.5)	6 (0.9)	0.388	2.02 (0.72–5.69)

ABC indicates Atrial Fibrillation Better Care.
*Between-group comparison made by $\chi 2$ test.
†Adjusted for age.
‡Composite outcome of all-cause death/any thromboembolism.

Likewise, multimorbidity and polypharmacy were associated with a preferential use of direct OACs in favor of vitamin K antagonists in those following the ABC pathway. Although the rhythm management strategies were scarcely used in the ChiOTEAF population,[38] they were more readily used in the ABC arm compared with the non-ABC arm. Furthermore, the use of the ABC pathway was associated with better health-related quality of life.

Consequently, adherence to the ABC pathway was associated with statistically lower rates of the composite outcome, all-cause mortality, and thromboembolic events in patients with AF with multimorbidity or polypharmacy and those with both multimorbidity and polypharmacy. There was no evidence to suggest that adhering to the ABC pathway was associated with a higher risk of major bleeding events compared with standard practice in any of the subgroups studied; indeed, when compared with the overall multimorbidity group, the bleeding risks were significantly lower in the ABC-managed multimorbidity group.

However, special attention should be paid to those with coronary artery disease, prior major bleeding, chronic kidney disease, and chronic obstructive pulmonary disease. Indeed, these comorbidities independently predict lower adherence to the ABC pathway. Prior major bleeding should not be a reason to withhold OAC, but mitigation of modifiable bleeding risks and regular review and follow-up of patients with high bleeding risk is required.[39–41] In our previous report, we demonstrated the efficacy of guideline-adherent OAC therapy among the elderly Chinese patients with AF.[42,43]

Favorable effects of the use of the ABC pathway are evident across various geographic regions, as various large-scale studies have demonstrated improvement in survival rates and reduction in cardiovascular events as a result of the ABC pathway implementation.[8,10,44] The mAFA-II trial, a cluster randomized trial, showed that the use of the ABC pathway was associated with a significantly lower risk of the composite outcome of stroke/thromboembolism, mortality, bleeding, and hospitalization compared with the usual care,[9] while the analysis of the long-term extension cohort demonstrated good adherence and persistence of use.[45] Of note, the ABC pathway is now recommended in international AF guidelines.[1,3]

Ongoing research demonstrates reproducible and generalizable results from systematic implementation of the ABC pathway are needed to address and help reduce nonadherence among physicians and patients alike.[46] We believe our study complements the existing knowledge base on the role and the utility of the ABC pathway in managing clinically complex patients by helping us further define its effectiveness and safety profile, particularly the noninferiority of the approach with regard to bleeding risk compared with standard practice.

Limitations

The primary limitation of the ChiOTEAF registry is its observational nature; the study was not designed to assess the role of the ABC pathway adherent care on patients' prognosis. ABC pathway adherence was assessed retrospectively on the basis of its definition published in 2017[7] and implemented into the 2020 European Society of Cardiology guideline.[1] We found that a moderate proportion of patients were lost to follow-up (9.3%), consistent with other large registries[47]; because of the limited availability of the data, only 56.2% of patients with multimorbidity and 58.7% of patients with polypharmacy were included in this analysis. To an extent, the observed associations of the ABC pathway with favorable clinical outcomes could have potentially been the result of patient self-selection rather than causal impact. Additionally, the data on ABC pathway adherence was available in only approximately half of the patients studied, which might have been a potential source of bias. Furthermore, the number of adverse clinical events, as well as AF-related procedures, may have been underreported. We did not report time-to-event data, and our outcomes were based on logistic regression. While competing risks of death may potentially impact on outcomes, our primary analysis focused on the OR of the composite outcome at 1 year. Finally, the data on anticoagulation monitoring and the use of traditional

Chinese medicines were not available and could not be considered in the analysis.

CONCLUSIONS

This nationwide real-world registry shows that adherence to the ABC pathway is associated with improved clinical outcomes and health-related quality of life in clinically complex Chinese patients with AF with multimorbidity or polypharmacy.

ARTICLE INFORMATION

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Disclosures

Dr Lip is a consultant and speaker for BMS/Pfizer, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are received personally. The remaining authors have no disclosures to report.

Supplemental Material

Appendix S1
Tables S1–S4

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SUPPLEMENTAL MATERIAL

Appendix S1. ChiOTEAF Registry Investigators

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Table S1. Predictors of the ABC compliance among patients with atrial fibrillation and multimorbidity.

	Univariate			Multivariate		
	Odds ratio	**95% CI**	**P**	**Odds ratio**	**95% CI**	**P**
Age	0.97	0.96-0.98	<0.001	0.98	0.97-0.99	<0.001
Female sex	1.01	0.93-1.27	0.317			
Diabetes mellitus	1.03	0.88-1.21	0.711			
Hypertension	1.58	1.32-1.89	<0.001	1.50	1.23-1.82	<0.001
Heart failure	0.82	0.70-0.96	0.014	-	-	-
Coronary artery disease	0.58	0.49-0.69	<0.001	0.55	0.46-0.65	<0.001
Prior ischemic stroke	1.11	0.93-1.31	0.242			
Prior major bleeding	0.11	0.05-0.23	<0.001	0.14	0.06-0.29	<0.001
Chronic kidney disease	0.58	0.46-0.75	<0.001	0.66	0.51-0.86	0.002
Liver disease	0.76	0.52-1.12	0.16			
COPD	0.58	0.44-0.76	<0.001	0.71	0.53-0.96	0.025
Sleep apnea	1.23	0.84-1.79	0.288			
Polypharmacy	1.87	1.59-2.18	<0.001	2.15	1.81-2.55	<0.001

CI – confidence interval; COPD – chronic obstructive pulmonary disease; OAC – oral anticoagulation.

Table S2. Effects of ABC compliance on clinical outcomes (composite outcome; all-cause death; any thromboembolism; major bleeding) among patients with multimorbidity and polypharmacy.

Outcomes	**ABC N=621** n (%)	**Non-ABC N=582** n (%)	**P^**	**Odds ratio*** (95% CI)
Composite outcome#	10 (1.6)	31 (5.3)	<0.001	0.38 (0.18-0.79)
All-cause death	7 (1.1)	18 (3.1)	0.017	0.49 (0.20-1.20)
TE events	4 (0.6)	15 (2.6)	0.007	0.31 (0.10-0.94)
Major bleeding	10 (1.6)	5 (0.9)	0.242	2.43 (0.81-7.26)

*Adjusted for age.

Composite outcome of all-cause death/any thromboembolism

^ Between-group comparison made by $\chi 2$ test

TE – thromboembolism; CI – confidence interval.

Table S3. The effects of ABC compliance on clinical outcomes (composite outcome; all-cause death; any thromboembolism; major bleeding) among overall multimorbidity cohort.

Outcomes	**ABC N=1133** n (%)	**Non-ABC N=3511** n (%)	**P^**	**Odds ratio*** (95% CI)
Composite outcome#	20 (1.8)	441 (12.6)	<0.001	0.19 (0.12-0.30)
All-cause death	13 (1.1)	377 (10.7)	<0.001	0.15 (0.09-0.27)
TE events	8 (0.7)	84 (2.4)	<0.001	0.39 (0.19-0.83)
Major bleeding	13 (1.1)	77 (2.2)	0.025	0.71 (0.39-1.29)

*Adjusted for age.

Composite outcome of all-cause death/any thromboembolism

^ Between-group comparison made by $\chi 2$ test

TE – thromboembolism; CI – confidence interval.

Table S4. The effects of ABC compliance on clinical outcomes (composite outcome; all-cause death; any thromboembolism; major bleeding) among overall polypharmacy cohort.

Outcomes	**ABC N=687** n (%)	**Non-ABC N=1575** n (%)	**P^**	**Odds ratio*** (95% CI)
Composite outcome#	11 (1.6)	173 (11.0)	<0.001	0.19 (0.10-0.36)
All-cause death	8 (1.2)	143 (9.1)	<0.001	0.18 (0.09-0.37)
TE events	4 (0.6)	36 (2.3)	0.003	0.35 (0.12-0.99)
Major bleeding	10 (1.5)	32 (2.0)	0.345	0.98 (0.47-2.05)

*Adjusted for age.

Composite outcome of all-cause death/any thromboembolism

^ Between-group comparison made by $\chi 2$ test

TE – thromboembolism; CI – confidence interval.