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CLINICAL RESEARCH
Atrial fibrillation

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

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Aims There has been an increasing focus on integrated, multidisciplinary, and holistic care in the treatment of atrial fibrillation (AF). The 'Atrial Fibrillation Better Care' (ABC) pathway has been proposed to streamline integrated care in AF. We evaluated the impact on outcomes of an ABC adherent management in a contemporary real-life European-wide AF cohort.

Methods and results Patients enrolled in the ESC-EHRA EURObservational Research Programme in AF General Long-Term Registry with baseline data to evaluate ABC criteria and available follow-up data were considered for this analysis. Among the original 11 096 AF patients enrolled, 6646 (59.9%) were included in this analysis, of which 1996 (30.0%) managed as ABC adherent. Patients adherent to ABC care had lower CHA_2DS_2-VASc and HAS-BLED scores (mean ± SD, 2.68 ± 1.57 vs. 3.07 ± 1.90 and 1.26 ± 0.93 vs. 1.58 ± 1.12, respectively; $P < 0.001$). At 1-year follow-up, patients managed adherent to ABC pathway compared to non-adherent ones had a lower rate of any thromboembolic event (TE)/acute coronary syndrome (ACS)/cardiovascular (CV) death (3.8% vs. 7.6%), CV death (1.9% vs. 4.8%), and all-cause death (3.0% vs. 6.4%) (all $P < 0.0001$). On Cox multivariable regression analysis, ABC adherent care

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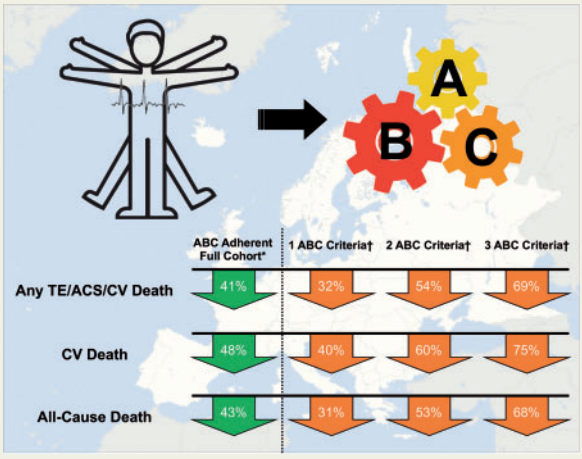
showed an association with a lower risk of any TE/ACS/CV death [hazard ratio (HR): 0.59, 95% confidence interval (CI): 0.44–0.79], CV death (HR: 0.52, 95% CI: 0.35–0.78), and all-cause death (HR: 0.57, 95% CI: 0.43–0.78).

Conclusion In a large contemporary cohort of European AF patients, a clinical management adherent to ABC pathway for integrated care is associated with a significant lower risk for cardiovascular events, CV death, and all-cause death.

Graphical Abstract



Keywords Atrial fibrillation • Integrated care • Outcomes • Registry

What's new?

- Integrated care is part of in atrial fibrillation (AF) management.
- The 'Atrial Fibrillation Better Care' (ABC) pathway has been proposed to streamline integrated care in AF patients.
- In a cohort of contemporary AF patients, an ABC adherent care was evident in 30.0% of patients.
- Clinical management adherent to ABC pathway was associated with a lower risk of cardiovascular events, cardiovascular death, and all-cause death.

Introduction

In recent years, the need for a more comprehensive management of patients diagnosed with atrial fibrillation (AF) has been advocated, which would go beyond the 'mere' prescription of oral anticoagulant (OAC) drugs for the management of thromboembolic risk.[1–3] Indeed, several studies clearly underline the increased risk of death in patients with AF, particularly cardiovascular (CV) death, also in relationship to the changing epidemiology of AF and the associated burden of comorbidity.[4–8] Hence, the introduction of different clinical strategies would apply an 'integrated care' approach with the final aim to reduce the entire spectrum of possible adverse outcomes.[1,2]

While initial evidence underlines how a more integrated care approach seems to be able to reduce the risk of all-cause death and hospitalization,[9,10] the biggest issue in developing a more modern and simple clinical strategy is currently the way to best operationalize this integrated care approach, and the need for more data coming from focused analyses and specific studies to investigate the impact of this approach.

The 'ABC' (Atrial Fibrillation Better Care) pathway was proposed as possible alternative to streamline the development and application of an integrated care management strategy.[11] The ABC pathway is based on three pivotal pillars: (A) *A*nticoagulation/Avoid stroke, i.e. optimizing treatment with OAC; (B) *B*etter symptom management with patient-centred decisions on rate or rhythm control; (C) *C*ardiovascular and other *C*omorbidities management with the optimal medical therapy, including lifestyle changes.[11] Since that, several papers have explored the possible usefulness of an ABC adherent management strategy in reducing the risk of adverse outcomes in AF patients, showing encouraging results.[12–14]

In this report from the European Society of Cardiology (ESC) EURObservational Research Programme (EORP) Atrial Fibrillation General Long-Term Registry, we evaluated if an ABC adherent management strategy would be useful to reduce the risk of adverse outcomes in a European-wide contemporary prospective cohort of AF patients managed by cardiologists.

Methods

The ESC-EORP Atrial Fibrillation General Long-Term Registry is a multicentre observational registry held by the ESC and endorsed by the European Heart Rhythm Association (EHRA). The General Long-Term Registry has been preceded by the General Pilot Registry.[5,15–17] The overall aim of the two registries was to provide real-world European-wide data about epidemiology, clinical characteristics, and management of AF patients in a contemporary cohort. The General Long-Term Registry was held in 27 ESC countries, enrolling consecutive AF patients in 250 cardiology practices. The detailed description of study design and main follow-up data were reported elsewhere.[18,19] All patients enrolled had AF documented within 12 months before enrolment on the basis of objective electrocardiographic evaluation, were ≥18 years old and provided written informed consent form. Enrolment was undertaken from October 2013 to September 2016, while 1-year follow-up was performed up until to September 2017. Institutional review board approved the study protocol for every institution, and the study was performed according to the EU Note for Guidance on Good Clinical Practice CPMP/ECH/135/95 and the Declaration of Helsinki.[18]

Thromboembolic risk was defined according to CHA_2DS_2-VASc score.[1] 'Low risk' was defined as a CHA_2DS_2-VASc 0 in males and 1 in females; 'moderate risk' was defined for a CHA_2DS_2-VASc 1 in males; 'high risk' was defined as CHA_2DS_2-VASc ≥2. Bleeding risk was defined according to HAS-BLED score.[1] 'Low risk' was defined as HAS-BLED 0–2, while 'high risk' was defined as HAS-BLED ≥3. Symptomatic status was defined according to EHRA score.[1]

Atrial Fibrillation Better Care pathway evaluation

According to its original definition, the ABC pathway was evaluated as follows:

'A' Criterion: A patient would qualify for this criterion if properly prescribed and treated with an OAC according to thromboembolic risk. Treatment with a vitamin K antagonist (VKA) and a time in therapeutic range (TTR) ≥70% or a non-vitamin K antagonist oral anticoagulant (NOAC) was considered as optimal treatment in male patients with CHA_2DS_2-VASc ≥1 or female patients with CHA_2DS_2-VASc ≥2; patients not qualifying for OAC therapy (i.e. CHA_2DS_2-VASc 0 in males or 1 in females) and not treated with OAC, also qualified for the 'A' criterion.

'B' Criterion: Any patient with an EHRA score of I (no symptoms) or II (mild symptoms not affecting daily life) qualified for this criterion. The 'B' criterion refers to the actual symptoms control, which is considered pivotal, rather than the *attempt* to control the symptomatic presentation.

'C' Criterion: To evaluate the adherence to the 'C' criterion, we considered the most frequent comorbidities associated with AF: hypertension, coronary artery disease, peripheral artery disease, heart failure, stroke/transient ischaemic attack, and diabetes mellitus. A patient qualified for the 'C' criterion when affected with ≥1 of these conditions and prescribed/treated according to the best medical treatment defined according to the current clinical guidelines. Optimal medical treatment was defined as follows: (i) for hypertension, we considered controlled blood pressure if ≤140/90 mmHg was recorded at baseline; (ii) for coronary artery disease, treatment with angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, and statins; (iii) for peripheral artery disease, treatment with statins; (iv) for previous stroke/transient ischaemic attack, treatment with statins; (v) for heart failure, we considered treatment with ACE inhibitors/angiotensin receptor blockers and beta-blockers; (vi) for diabetes mellitus, treatment with insulin or oral antidiabetics. In the case of clinical history for ≥1 condition considered; the patient needed to be properly treated for all the conditions to qualify for the 'C' criterion.

A patient was considered as fully ABC pathway adherent ('ABC adherent care') if all the three criteria were fulfilled, otherwise the patient was considered as being managed with an ABC non-adherent care. Furthermore, we evaluated the number of ABC criteria fulfilled.

Adverse outcomes

Adverse outcomes were considered at the 1-year follow-up observation. During follow-up, all incident major adverse clinical events were recorded, with the composite outcome of any thromboembolism (TE) (including stroke, transient ischaemic attack, and any peripheral embolism)/acute coronary syndrome (ACS)/CV death, CV death, all-cause death as the main study outcomes. We also considered the individual outcomes of stroke, any TE, any haemorrhagic events, and intracranial haemorrhage. Haemorrhagic events were not specifically defined, but all significant events which investigators became aware, were reported. All data about hospital admissions (any admission, AF-related, and CV-related) were also recorded. Investigators reported all available details about incident major adverse clinical events on the centralized electronic case report form. Events were recorded according to ABC adherent/non-adherent care and number of ABC criteria.

Statistical analysis

All continuous variables were reported as mean (standard deviation, SD) or as median and interquartile range. Kruskal–Wallis analysis of variance test was used accordingly. Categorical variables were reported as counts and percentages. Among-group comparisons were made using a χ^2 test or Fisher's exact test (if any expected cell count was <5). Further, differences in outcomes between groups were expressed as risk ratio and confidence interval (CI), as suggested by Altman.[20] Plots of Kaplan–Meier curves for time to any TE/ACS/CV death, to CV deaths or to all-cause of death according to antithrombotic pattern were performed. Survival distributions were compared using the log-rank test.

A univariate and multivariable logistic regression analysis for ABC adherent vs. ABC non-adherent care respect to all study outcomes was performed. Type of AF and CHA_2DS_2-VASc score factors were used as adjustments for every outcome except for haemorrhagic events and intracranial haemorrhage for which HAS-BLED score factors, sex, and type of AF were used. Results were expressed as odds ratio (OR) and 95% CI.

A univariate and stepwise multivariable Cox regression analysis, adjusted for all the main outcomes predictors in AF patients, was performed to establish the relationship between ABC adherent vs. ABC non-adherent and the risk of the composite outcome of any TE/ACS/CV death, CV death, or all-cause death. Into the model, all the candidate variables (variables with $P < 0.10$ in univariate) were included. A univariate significance level of 0.05 was required to allow a variable into the model (SLENTRY = 0.05) and a multivariate significance level of 0.05 was required for a variable to stay in the model (SLSTAY = 0.05). Hosmer and Lemeshow Goodness-of-Fit test was used to verify that the models were optimal. Results were expressed as hazard ratio (HR) and 95% CI. A two-sided $P < 0.05$ was considered statistically significant. All analyses were performed using SAS statistical software version 9.4 (SAS Institute, Inc., Cary, NC, USA).

Results

Among the 9663 AF patients enrolled into the ESC-EHRA EORP Atrial Fibrillation General Long-Term Registry and with available 1-year follow-up data,[19] a total of 6646 (68.8%) with available data to evaluate ABC pathway were included in this analysis. Patients not included in this analysis were found to be older (mean ± SD age

Table 1 Baseline characteristics according to ABC pathway status

	ABC Non-adherent N = 4650	ABC adherent N = 1996	P
Demographics			
Age (years), median (IQR)	69 (61–77)	70 (61–76)	0.2184
Female, *n* (%)	1926 (41.4)	741 (37.1)	0.0011
Type of AF, *n* (%)			0.0319
First diagnosed	935 (20.5)	438 (22.2)	
Paroxysmal	1365 (29.9)	523 (26.5)	
Persistent	939 (20.6)	414 (21.0)	
LS persistent	180 (3.9)	96 (4.9)	
Permanent	1139 (25.0)	500 (25.4)	
Concomitant diseases			
Hypertension, *n* (%)	2693 (58.5)	1184 (59.7)	0.3785
CAD, *n* (%)	1364 (31.0)	302 (15.9)	<0.0001
Previous MI, *n* (%)	590 (43.3)	161 (53.3)	0.0015
Heart failure, *n* (%)	1785 (38.8)	524 (26.4)	<0.0001
Valvular disease, *n* (%)	2031 (44.7)	846 (43.2)	0.2812
Dilated cardiomyopathy, *n* (%)	316 (6.9)	144 (7.3)	0.5762
Hypertrophic cardiomyopathy, *n* (%)	142 (3.1)	38 (1.9)	0.0072
Restrictive cardiomyopathy, *n* (%)	8 (0.2)	4 (0.2)	0.7615
Other cardiomyopathy, *n* (%)	155 (3.4)	61 (3.1)	0.5463
Congenital heart disease, *n* (%)	57 (1.2)	13 (0.7)	0.0339
PAH, *n* (%)	282 (6.2)	75 (3.8)	<0.0001
Cardiovascular risk factors			
Diabetes mellitus, *n* (%)	1091 (23.6)	321 (16.2)	<0.0001
Lipid disorder, *n* (%)	1790 (40.2)	720 (37.6)	0.0512
Current Smoker, *n* (%)	426 (9.8)	196 (10.3)	0.5879
No regular exercise, *n* (%)	1620 (40.5)	638 (36.1)	0.0017
Other comorbidities			
Previous stroke, *n* (%)	291 (6.3)	80 (4.0)	0.0002
Previous TIA, *n* (%)	173 (3.8)	35 (1.8)	<0.0001
Previous bleedings, *n* (%)	291 (6.3)	84 (4.2)	0.0007
PAD, *n* (%)	406 (8.9)	69 (3.5)	<0.0001
Chronic kidney disease, *n* (%)	585 (12.6)	155 (7.8)	<0.0001
COPD, *n* (%)	365 (7.9)	141 (7.1)	0.2554
Malignancy, *n* (%)	409 (8.9)	142 (7.2)	0.0208
Thyroid disease/disorder, *n* (%)	638 (14.0)	258 (13.1)	0.3454
Main reason for admission, *n* (%)			<0.0001
AF	3228 (69.4)	1516 (76.0)	
ACS	203 (4.4)	44 (2.2)	
Valvular disease	88 (1.9)	29 (1.5)	
Hypertension	90 (1.9)	43 (2.2)	
Heart failure	398 (8.6)	122 (6.1)	
Other CAD	124 (2.7)	34 (1.7)	
Other CV	319 (6.9)	126 (6.3)	
Other non-CV	200 (4.3)	82 (4.1)	
Symptomatic status, *n* (%)			<0.0001
EHRA I	1801 (38.7)	1035 (51.9)	
EHRA II	1534 (33.0)	961 (48.1)	
EHRA III–IV	1315 (28.3)	–	
Thromboembolic risk			
CHA_2DS_2-VASc, mean (SD)	3.07 (1.90)	2.68 (1.57)	<0.0001

Continued

Table 1 *Continued*

	ABC Non-adherent	ABC adherent	P
	N = 4650	N = 1996	
CHA_2DS_2-VASc, median (IQR)	3 (2–4)	3 (2–4)	<0.0001
Risk categories, *n* (%)			<0.0001
Low risk	683 (14.7)	205 (10.3)	
Moderate risk	406 (8.7)	274 (13.7)	
High risk	3561 (76.6)	1517 (76.0)	
Bleeding risk			
HAS-BLED, mean (SD)	1.58 (1.12)	1.26 (0.93)	<0.0001
HAS-BLED, median (IQR)	2 (1–2)	1 (1–2)	<0.0001
Risk categories, *n* (%)			<0.0001
Low-moderate risk	3747 (80.6)	1829 (91.6)	
High risk	903 (19.4)	167 (8.4)	

ABC, Atrial Fibrillation Better Care; ACS, acute coronary syndrome; AF, atrial fibrillation; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CV, cardiovascular; EHRA, European Heart Rhythm Association; IQR, interquartile range; LS, long-standing; MI, myocardial infarction; PAD, peripheral artery disease; PAH, pulmonary arterial hypertension; SD, standard deviation; TIA, transient ischaemic attack.

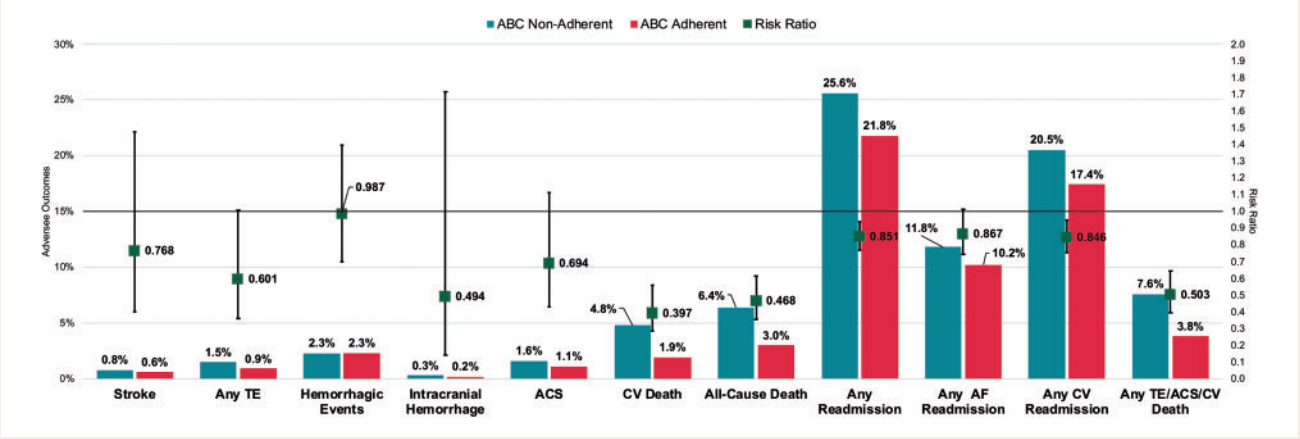


Figure 1 Adverse outcomes according to ABC pathway status. Differences between ABC adherent vs. ABC non-adherent management for stroke $P = 0.4261$, any TE $P = 0.0505$, haemorrhagic events $P = 0.9420$, intracranial haemorrhage $P = 0.2567$, ACS $P = 0.1277$, CV death $P < 0.0001$, all-cause death $P < 0.0001$, any readmission $P = 0.0011$, any AF readmission $P = 0.0685$, any CV readmission $P = 0.0035$, any TE/ACS/CV death $P < 0.0001$; green squares and whiskers stand for risk ratio and 95% CI. ABC, Atrial Fibrillation Better Care; ACS, acute coronary syndrome; AF, atrial fibrillation; CI, confidence interval; CV, cardiovascular; TE, thromboembolic event.

71.4 ± 10.0 vs. 68.3 ± 12.0 in patients included in the analysis, $P < 0.0001$) and with a higher thromboembolic [mean CHA_2DS_2-VASc 3.53 (SD 1.65) vs. 2.95 (SD 1.81), $P < 0.0001$] and bleeding risk [mean HAS-BLED 1.74 (SD 1.05) vs. 1.48 (SD 1.08), $P < 0.0001$]. Amongst the patients included in the analysis, 1,996 (30.0%) patients qualified for all the three ABC criteria and therefore were fully managed with an ABC adherent care. Furthermore, 1276 (19.2%) patients qualified for only 1 ABC pathway criterion, while 3219 (48.4%) qualified for 2 ABC criteria.

Baseline characteristics for ABC non-adherent vs. ABC adherent care were reported in *Table 1*. Patients managed with an ABC adherent care were less likely to be female or to have various CV and non-CV comorbidities compared to those treated with ABC non-adherent care, while there was no significant difference in age. Patients treated with an ABC adherent care had a significantly lower CHA_2DS_2-VASc and HAS-BLED scores.

During the 1-year follow-up, there were 422 (6.4%) events of the composite outcome (any TE/ACS/CV Death), 261 (3.9%) CV deaths, and 359 (5.4%) all-cause deaths recorded. Adverse outcomes according to ABC adherent and ABC non-adherent care are shown in *Figure 1*. There was a significant reduction in all the main study outcomes amongst ABC adherent care managed patients, with a 50%

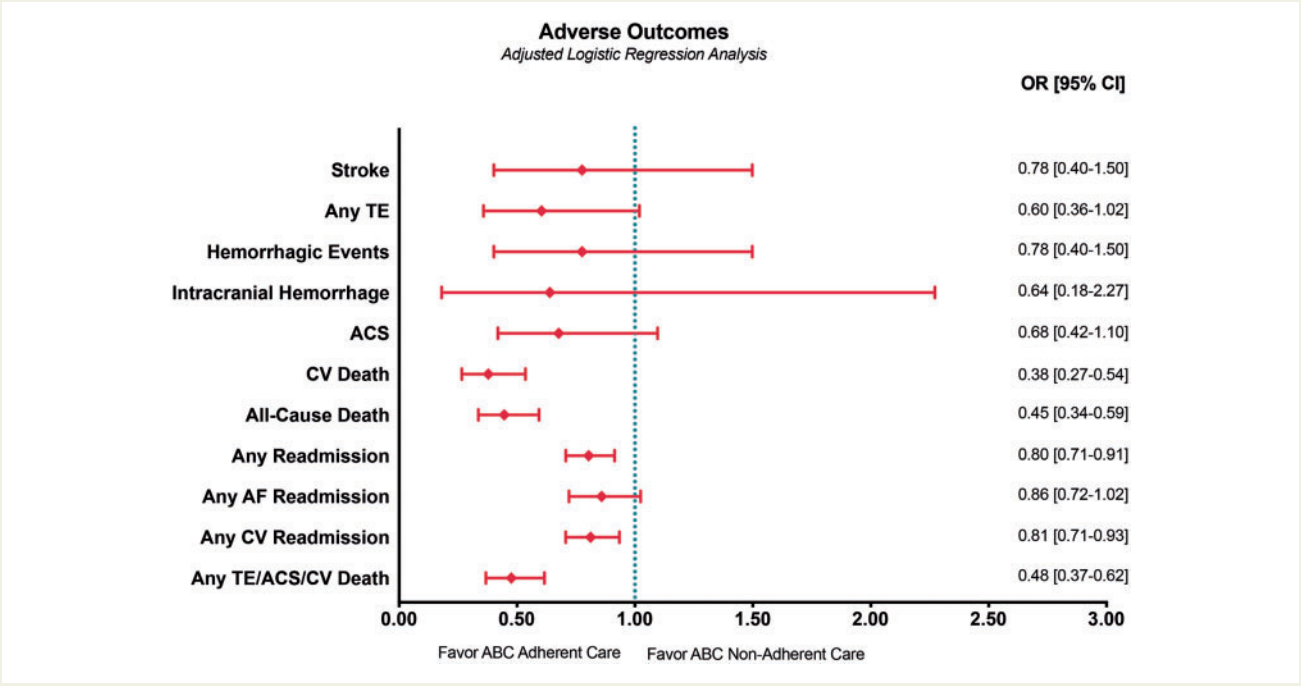


Figure 2 Multivariate adjusted logistic regression analysis for ABC pathway status and adverse outcomes. ABC, Atrial Fibrillation Better Care; ACS, acute coronary syndrome; AF, atrial fibrillation; CI, confidence interval; CV, cardiovascular; OR, odds ratio; TE, thromboembolic event.

lower risk for any TE/ACS/CV death, a 60% lower risk for CV death, and a 55% lower risk for all-cause death (*Figure 1*). There was a significantly lower rate for any readmission and any CV readmission outcomes in patients managed with ABC adherent care, when compared with ABC non-adherent care (*Figure 1*).

On multivariable adjusted logistic analysis (*Figure 2*), ABC adherent care was independently associated with a lower risk of CV death, all-cause death, any readmission, any CV readmission, and any TE/ACS/CV death, with non-statistically significant trends in lower risk for any TE and any AF readmission.

Kaplan–Meier curves analysis (*Figure 3*) showed a higher cumulative survival for ABC adherent care in all the three main study outcomes (*Figure 3A, C*, and *E*). Furthermore, when examined according to the number of ABC pathway criteria there was a progressively lower cumulative survival for the three main study outcomes with progressively lower number of ABC criteria fulfilled (*Figure 3B, D*, and *F*).

The final multivariable adjusted Cox regression analysis (*Table 2*) showed that the use of an ABC adherent care was independently associated with a lower risk for the three main study outcomes, with up to 50% risk reduction for CV death occurrence. A progressively higher number of ABC criteria fulfilled was independently associated with a progressively lower risk for all the three outcomes occurrence.

Discussion

In this report from the ESC-EORP Atrial Fibrillation General Long-Term Registry, we show that in a European real-life contemporary cohort of AF patients, clinical management adherent to the ABC pathway was associated to a significant reduction in risk for the composite outcome of any TE/ACS/CV death, CV death, and all-cause death. Second, an increasing number of ABC criteria fulfilled was associated with a progressively lower risk for all the three main study outcomes.

Thus far, the studies investigating the impact of an ABC adherent care showed a consistent association with a lower risk of all-cause death, CV death,[12,14] and CV events.[12,13] In this contemporary European cohort of AF patients, we found a strong significant association with a reduced risk for CV events, CV death, and all-cause death. Prior studies comparing integrated care approaches have documented a reduced risk of all-cause death and CV death.[9,21,22] In the *post hoc* analysis derived from a randomized clinical trial, for example, comparing a multidisciplinary integrated AF-clinic with usual care, an integrated care management approach was associated with >50% risk reduction (HR: 0.44, 95% CI: 0.23–0.85), with also a significant reduction in CV death (HR: 0.28, 95% CI: 0.09–0.85),[21] after up to 2 years of follow-up.

Furthermore, we showed a significant association with a reduced risk for hospital readmissions, in particular, CV-related hospitalization. This finding is again aligned with other studies showing a significant reduction of hospitalizations or emergency department admissions risk in groups of patients managed with an integrated care approach.[9,12,22]

The logistic regression analysis did not show a significant reduction in risk of thromboembolic and bleeding events for the ABC adherent care. These may reflect lower statistical power, but these results were also consistent with those reported in other studies.[12] A recent

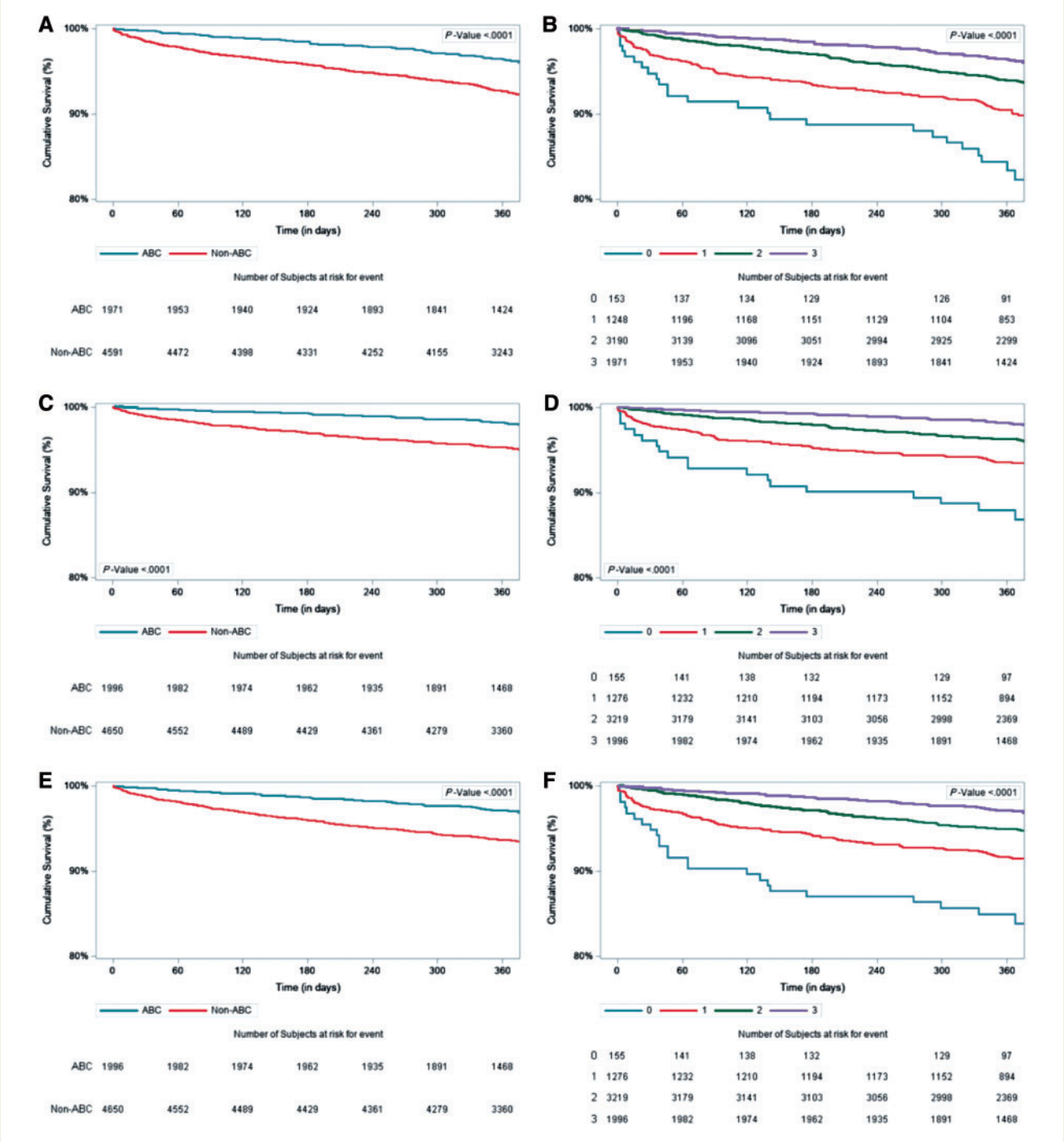


Figure 3 Kaplan–meier curves for main study outcomes according to ABC pathway status and number of ABC criteria. (*A*) Any TE/ACS/CV Death Risk according to ABC pathway status; (*B*) any TE/ACS/CV death risk according to number of ABC criteria; (*C*) CV death risk according to ABC pathway status; (*D*) CV death risk according to number of ABC criteria; (*E*) all-cause death risk according to ABC pathway status; (*F*) all-cause death risk according to number of ABC criteria. ABC, Atrial Fibrillation Better Care; ACS, acute coronary syndrome; AF, atrial fibrillation; CI, confidence interval; CV, cardiovascular; OR, odds ratio; TE, thromboembolic event.

randomized controlled trial (mAFA trial) implementing the ABC pathway in an Asian population showed a significant reduction in the composite outcome of thromboembolic events (TEs)/rehospitalization/all-cause death in the short term, but did not found any significant reduction in TEs and bleeding events.[23] We would hypothesize that these results could be due by the very low rate of

Table 2 Cox regression multivariable analysis for ABC adherent care about adverse outcomes

	Any TE/ACS/CV death[a]	CV death[b]	All-cause death[c]
	HR (95% CI)	HR (95% CI)	HR (95% CI)
ABC non-adherent	Ref.	Ref.	Ref.
ABC adherent	0.59 (0.44–0.79)	0.52 (0.35–0.78)	0.57 (0.43–0.78)
No ABC criteria	Ref.	Ref.	Ref.
1 ABC criteria	0.68 (0.42–1.10)	0.60 (0.33–0.94)	0.69 (0.42–1.14)
2 ABC criteria	0.46 (0.29–0.74)	0.40 (0.24–0.66)	0.47 (0.29–0.76)
3 ABC criteria	0.31 (0.19–0.52)	0.25 (0.14–0.45)	0.32 (0.18–0.54)

ABC, Atrial Fibrillation Better Care; ACS, acute coronary syndrome; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; TE, thromboembolic event.
[a]Multivariable analysis showed the impact of ABC adherent treatment independently of increasing age, hypertension, diabetes mellitus, coronary artery disease (CAD), stroke/transient ischaemic attack, heart failure, peripheral vascular disease (PAD), chronic kidney disease (CKD), and reason for admission.
[b]Multivariable analysis showed the impact of ABC adherent treatment independently of increasing age, CAD, heart failure, PAD, CKD, malignancy, and reason for admission.
[c]Multivariable analysis showed the impact of ABC adherent treatment independently of increasing age, type of atrial fibrillation, heart failure, any cardiomyopathy, CKD, hypercholesterolaemia, malignancy, and reason for admission.

both thromboembolic and bleeding events, since the present and prior studies were not powered or had long enough follow-up to identify differences in those individual outcomes.

The results we presented are particularly relevant in epidemiological terms, in relation to the study cohort from which the data were derived. First, the original cohort represents the largest observational industry-independent study about AF care in Europe, including patients from 27 European countries. Second, data we presented reflect contemporary AF epidemiology and management, compared to previous studies investigating the impact of ABC adherent management strategies that investigated older or limited cohorts, or those which were restricted to Asian patients.[12–14] Third, this cohort represents the largest number of AF patients managed with an ABC adherent care approach, providing reliable results in terms of number of patients and events. The evidence that an increasing number of ABC criteria fulfilled showed an association with a progressively lower risk of adverse outcomes further corroborates the concept that if patient management was increasingly adherent to the ABC pathway, there would be a larger clinical benefit obtained.

Indeed, our article emphasizes how a management strategy based on integrated care would be crucial to reduce the risk of adverse outcomes in AF patients. It is now established how AF patients are progressively more burdened with comorbidities,[1,8] which determine the occurrence of all-cause death and CV death in AF patients.[4,8] One recent study explored the hypothesis that presence of AF could represent a proxy for an increased risk of multimorbidity and how AF patients reported a progressively increasing risk of adverse outcomes according to a progressively increasing level of multimorbidity.[24] To properly manage such a burden of concomitant conditions, it appears evident how a 'single-disease' strategy or 'single management'; strategy would not be the most suitable approach to obtain a significant reduction of adverse outcomes. Indeed, implementation of a simple, effective, and easily operationalizable integrated care approach would be pivotal especially since AF is managed by a broad spectrum of healthcare professionals, including general practitioners, emergency room physicians, non-cardiologists (emergency room physicians, surgeons, intensive care unit specialists, and geriatricians), and cardiologists (interventionists, electrophysiologists); but central to all is the patient and their carers, who need a uniform simple and consistent message of AF management ('Easy as ABC . . .').

Limitations

The main limitation of the study is related to its observational nature, with a limited power to detect differences in subgroups not prespecified in the study design. The differences in baseline characteristics between patients included and not included in the analysis could introduce some limitation to the generalization of the results, even though the cohort analysed represents almost 70% of the patients with available follow-up and patients were included exclusively on the data availability, given the observational cohort design. Requiring the availability of TTR for patients treated with VKA, which was not mandatory to be collected, it is very likely the missing data about this covariate influenced the availability of patients for this analysis. Even though the outcome events were not centrally adjudicated, this limitation is shared by almost all real-life observational registries. Despite the multivariable analysis demonstrated the independent association between ABC adherent care and lower risk of outcomes, there may still exist residual bias given differences in patients' risk profile or follow-up management, as the presence of other comorbidities not captured in the study case report form or included in the 'C' criterion, adherence and persistence to pharmacological treatment as well as the absence of clinical metrics that could allow us to measure the response to pharmacological treatment of the comorbidities considered. Another limitation is related to the study setting, based exclusively on European cardiology practices. Since AF patients are also commonly managed by different health professionals, our data need to be cautiously interpreted when extended to the entire general AF population.

Lastly, the data presented do not imply causality, rather to describe an association. Despite the multivariable analysis being performed

with a large set of covariates, the differences in baseline characteristics between the subjects managed with an ABC adherent care and those not managed adherent to ABC pathway cannot allow us to make an inference of causality. Even though exist modelling statistical techniques to adjust for differences in baseline characteristics (e.g. propensity score matching, inverse probability treatment weighting), we do believe that these techniques could not be used given the nature of the study and the composite nature of the exposure (i.e. ABC adherent care).

Hence, our data should be considered as a 'proof-of-concept' study, with the need for prospective data collected through specifically designed and adequately powered prospective studies.[23]

Conclusions

In a large contemporary cohort of European AF patients, a clinical management adherent to ABC pathway for integrated care was associated with a significant lower risk for cardiovascular events, CV death, and all-cause death. An increasing number of ABC criteria fulfilled was associated with a progressively lower risk of the main clinical outcomes.

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Data availability

The data underlying this article were provided by the European Society of Cardiology by permission. Data will be shared on request to the corresponding author with permission of ESC Editorial is also expected but not yet confirmed.

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Giant left atrial calcified myxoma-induced premature atrial contractions

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A 73-year-old woman with palpitations for 3 months was referred for a diastolic murmur and frequent premature atrial contractions (PACs) (21,544 PACs/day). During the PACs, the P-wave morphology was negative/positive in lead V1 and positive in lead aVL (*Panel A*), suggesting their origin in the septal left atrium (LA). Transthoracic echocardiography showed a mass in the LA; cardiac computed tomography demonstrated a giant calcified mass with a stalk to the LA septum (*Panel B*). After surgical resection of the mass, histopathology confirmed a rare calcified myxoma, and the PACs were disappeared. At 18 months of follow-up, the patient was free of any atrial arrhythmias.