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Compliance of atrial fibrillation treatment with the ABC pathway in patients with concomitant diabetes mellitus in the Middle East based on the Gulf SAFE registry

Magdalena Domek[1,2] | **Jakub Gumprecht**[1,3] | **Yan-Guang Li**[4] | **Marco Proietti**[1,5,6] | **Wafa Rashed**[7,8] | **Ahmed Al Qudaimi**[9] | **Janusz Gumprecht**[2] | **Mohammad Zubaid**[7,8,10] | **Gregory Y. H. Lip**[1,3,11]

[1]Liverpool Centre for Cardiovascular Science, University of Liverpool and Liverpool Heart & Chest Hospital, Liverpool, UK

[2]Department of Internal Diseases, Diabetology and Nephrology, Medical University of Silesia, Zabrze, Poland

[3]Department of Cardiology, Silesian Centre for Heart Diseases, Medical University of Silesia, Zabrze, Poland

[4]Department of Cardiology, Peking University Third Hospital, Beijing, China

[5]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

[6]Geriatric Unit, Fondazione IRCCS Ca'Granda, Ospendale Maggiore Policlinico, Milan, Italy

[7]Department of Medicine, Mubarak Al-Kabeer Hospital, Kuwait

[8]Division of Cardiology, Mubarak Al-Kabeer Hospital, Kuwait, Kuwait

[9]AlThawra Hospital, Sana'a, Yemen

[10]Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait, Kuwait

[11]Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

Correspondence
Gregory Y. H. Lip, Liverpool Centre for Cardiovascular Science, University of

Abstract

Introduction: Atrial fibrillation (AF) and diabetes mellitus (DM) constitute a heavy burden on healthcare expenditure due to their negative impact on clinical outcomes in the Middle East. The Atrial fibrillation Better Care (ABC) pathway provides a simple strategy of integrated approach of AF management: A—Avoid stroke; B—Better symptom control; C—Cardiovascular comorbidity risk management.

Aims: Evaluation of the AF treatment compliance to ABC pathway in DM patients in the Middle East. Assessment of the impact of ABC pathway adherence on all-cause mortality and the composite outcome of stroke/systemic embolism, all-cause death and cardiovascular hospitalisations.

Methods: From 2043 patients in the Gulf SAFE registry, 603 patients (mean age 63; 48% male) with DM were included in an analysis of ABC pathway compliance: A—appropriate use of anticoagulation according to CHA_2DS_2-VASc score; B—AF symptoms management according to the European Heart Rhythm Association (EHRA) scale; C—Optimised cardiovascular comorbidities management.

Results: 86 (14.3%) patients were treated in compliance with the ABC pathway. During 1-year follow-up, 207 composite outcome events and 87 deaths occurred. Mortality was significantly lower in the ABC group vs non-ABC (5.8% vs 15.9%, $P = .0014$, respectively). On multivariate analysis, ABC compliance was associated with a lower risk of all-cause death and the composite outcome after 6 months (OR 0.18; 95% CI: 0.42-0.75 and OR 0.54; 95% Cl: 0.30-1.00, respectively) and at 1 year (OR 0.30; 95% Cl: 0.11-0.76 and OR 0.57; 95% Cl: 0.33-0.97, respectively) vs the non-ABC group.

Zubaid and Lip joint senior authors.

Liverpool and Liverpool Heart & Chest Hospital, Liverpool, UK.
Email: gregory.lip@liverpool.ac.uk

Conclusions: Compliance with the ABC pathway care was independently associated with the reduced risk of all-cause death and the composite outcome in DM patients with AF, highlighting the importance of an integrated approach to AF management.

KEYWORDS
ABC pathway, all-cause death, anticoagulation, atrial fibrillation, stoke

1 | INTRODUCTION

Atrial Fibrillation (AF) is a leading cause of cardiovascular death as well as disability and impaired quality of life by exacerbating other underlying comorbidities such as heart failure, stroke or dementia.[1-5] Furthermore, AF is a growing epidemic is associated with high costs of treatment and hospitalisations, thus having significant implications for healthcare costs.[4,6,7]

Similarly, for diabetes mellitus (DM), the latest estimates show a steadily increasing trend in the numbers of such patients. By the end of 2045, the number of DM patients is expected to reach 700 million, which represents an increase by around 40%.[8] Indeed, the Middle East is one of the world's regions where the growth of people with diabetes is predicted to be the largest over the next few years, and the prevalence is increasing[8] This is even more important given that DM is a well-established risk factor for many cardiovascular diseases, including AF.[9,10] Many studies report the common coexistence of AF and DM, and their associated cardiovascular risks.[7,11-15] Hence, patients with DM are not only more likely to develop AF during their life, but they also have a significantly higher overall risk of cardiovascular complications.[16,17]

Given the multifactorial background of AF, a more integrated and holistic approach to AF management with optimised drug therapies may improve clinical outcomes.[18-20] The Atrial fibrillation Better Care (ABC) pathway for integrated care of AF patients is a simple strategy showing step-by-step how to approach AF management in a comprehensive and sensible way.[5] The ABC pathway refers to the following steps: Avoid stroke with Anticoagulation (A); Better symptom management with patient-centred symptom-directed decisions on rate or rhythm control (B); Cardiovascular and comorbidity risk optimisation (C). The 'A' criterion refers to optimisation of stroke prevention, which involves initial identification of low-risk patients, who are not recommended any antithrombotic therapy. Following this, patients with ≥1 stroke risk factors are considered for OAC and would require assessment of bleeding risk and decision-making on OAC type.[5] The 'B' criterion refers to symptom assessment of the patient with AF and deciding the initial treatment strategy to be established with rate control drugs or rhythm control with antiarrhythmic drugs or electrophysiological procedures. The 'C' criterion refers to effective management of comorbidities as well as patient involvement with lifestyle changes, dietary habits or physical activity.[5] The above-mentioned holistic care approach facilitates risk reduction through effective treatment of accompanying diseases, whereby DM is one of the most prominent examples.[5]

Novelty statement

- Most AF patients with diabetes are not optimally treated despite having a high risk of stroke.
- Integrated optimal treatment, according to the ABC pathway regimen, reduces the risk of all-cause mortality and composite outcome.
- The substantial mortality and composite outcome risk reduction in ABC compliant group is independent either of the duration of follow up and other adjusted risk factors.

In this study, we evaluated whether the management of AF patients with concomitant DM in the Middle East region was generally compliant with the ABC regimen, based on a 'real-world' dataset enrolled in the Gulf Survey of Atrial Fibrillation Events (Gulf SAFE registry). Second, the impact of ABC pathway compliant management on adverse clinical outcomes. The adherence to the ABC pathway and its impact on clinical outcomes has never been previously evaluated in this Middle Eastern population.

2 | METHODS

The Gulf SAFE dataset is a multi-centre, observational, prospective cohort study recording subsequent AF patients from 6 countries in the Gulf region of the Middle East. Details on the methods have been described in the previously published papers.[21] Briefly, the register consists of AF patients admitted to ER from 23 participating hospitals between October 15, 2009, and June 30, 2010, regardless of the primary reason for admission. The qualifying criterion was age over 18 years and the duration of AF >30 seconds on a 12-lead resting electrocardiogram. Consequently, the Gulf SAFE registry had 2043 participants. All patients gave informed

consent for their participation after being informed about the details of the study. The study received approval from the ethics committees of each institution/country and conforms to recognised standards. For the purposes of this study, we included only patients with AF and DM, and this cohort of 603 patients was analysed.

We analysed compliance in line with the ABC pathway components, which were defined on the basis of ESC Guidelines[22] as follows:

- *'A' -avoid stroke*: All AF patients with DM have a high risk of stroke (CHA_2DS_2-VASc score of ≥1 in men or ≥2 in women), and therefore, we assessed whether subjects were treated with OAC ('A compliant'). Those who did not receive OACs were considered as 'A noncompliant'. The vast majority of patients receiving OAC in the current study were administered with vitamin K antagonists (VKA eg warfarin).
- *'B- better symptoms control'*: We evaluated the occurrence of symptoms and classified them according to the European Heart Rhythm Association (EHRA) symptom scale. We assumed that patients with EHRA I or II had well-controlled AF symptoms ('B compliant') in comparison to those with EHRA III or IV, who were more symptomatic and treated insufficiently ('B noncompliant').
- *'C- Cardiovascular and other comorbidities'*: To reduce cardiovascular risk, we evaluated appropriate treatment(s) of the following comorbidities based on available data: hypertension (HT), coronary artery disease (CAD), peripheral artery disease (PAD), stroke/TIA. HT assessment was based on an average of blood pressure values at hospital admission that should be <140/90 mm Hg in order to be considered as well controlled. For other comorbidities, optimal pharmacologic management was evaluated in accordance with the current European guidelines and recommendations (Figure 1). 'C compliant' means that all comorbidities were either well-controlled or treated with appropriate prevention drugs or both. Finally, patients who met all criteria were defined as the 'ABC group', and those who did not meet all criteria were the 'Non-ABC' group.

2.1 | Outcomes

In our analysis, we assessed all-cause mortality and a *composite outcome*, which consists of the following events that occurred during follow-up: stroke or systemic embolism, all-cause death and cardiovascular hospitalisation. The primary analysis was a comparison of the above-mentioned outcomes between patients with integrated care management in accordance with the ABC pathway (ABC group), compared to those without ABC pathway compliance (non-ABC group).

2.2 | Statistical analysis

Continuous variables were reported as mean ± standard deviation and evaluated by Student's *t* test or Mann-Whitney, as necessary. Categorical variables were expressed as percentages and counts and compared using Pearson's chi-square test or Fisher's exact test, as appropriate. All the patients included a further assessment to have AF and DM. The major analyses were based on the comparison of the clinical outcomes between two study groups: ABC group vs the non-ABC group, whereby the former reflects compliance with the ABC pathway in AF management while the latter does not. The secondary analysis evaluated the impact of the total number of ABC steps fulfilled, the partial compliance with ABC regimen (0 or 1 ABC fulfilled criteria vs 2 of 3 fulfilled ABC criteria) and particular criteria met (A, B or C) on the major clinical outcomes, that is, all-cause mortality and composite outcome.

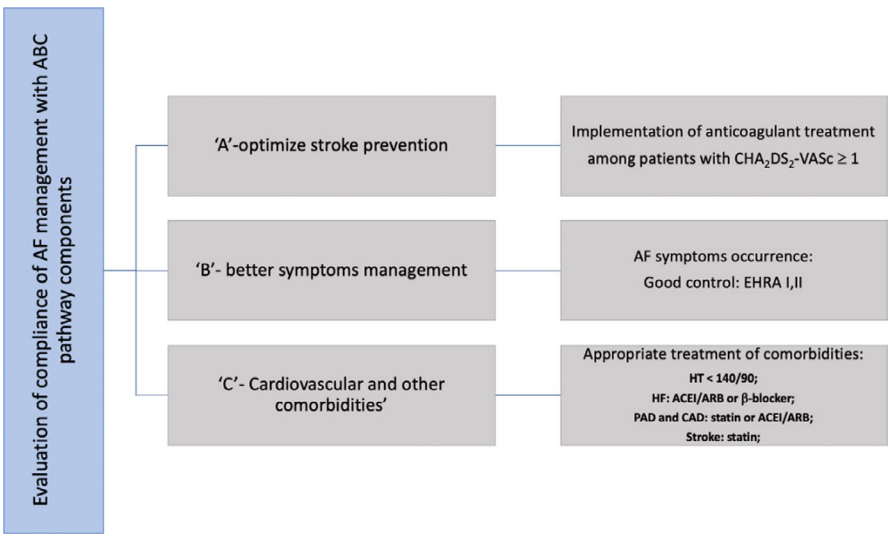

FIGURE 1 Methodology scheme of the evaluation of AF management compliance with ABC pathway components. For details, see text

Odds ratios (ORs) were analysed using multivariable logistic regression model and were used according to the outcomes considered. All multivariable regression models were adjusted for AF type, renal dysfunction, dyslipidemia, use of aspirin and major bleeding, which are well-known risk factors for all-cause mortality and the composite outcome components.

All tests were 2-sided and P value <.05 was considered as statistically significant. Analyses were performed with the SPSS version 24 software package (SPSS Inc).

3 | RESULTS

From 2043 patients with AF enrolled in the Gulf SAFE registry, there were 603 (30%) patients with concomitant DM, who were included in the analysis. Overall, 86 (14.3%) patients were treated optimally according to ABC pathway. Baseline characteristics of the study cohort are presented in Table 1. Patients from the ABC group and the non-ABC group did not significantly differ in terms of gender, age and BMI.

Compared to the non-ABC group, patients in ABC group had lower mean systolic and diastolic blood pressure (both $P < .001$), suffered more frequent due to chronic kidney disease ($P = .021$). Patients from ABC compliant group were also administered a larger number of medications (Table. 1).

3.1 | 'A' compliance and anticoagulation management

All 603 patients included in the analysis were at high stroke risk (CHA_2DS_2-VASc score ≥2 for women or ≥1 for men) therefore required anticoagulant therapy. There were 349 (57.9%) patients in the study cohort treated in line with 'A' (Table 2). Of these, 151 (25.1%) were treated with an OAC monotherapy, 142 (23.5%) received dual antithrombotic therapy and 25 (4.2%) received triple antithrombotic therapy, while 34 (5.6%) had no anticoagulant/antiplatelet therapy at all. A detailed description of OAC management is presented in Table S1.

3.2 | 'B' compliance and symptoms control

In the cohort, there were 441 (73.1%) well-managed patients with either EHRA I-II scores, who were categorised as B compliant. Of these, 182 (30.1%) patients were asymptomatic (EHRA I) and 259 (53.0%) had mild symptoms (EHRA ≤ 2), mostly palpitations (56.1%).

3.3 | *'C' compliance and comorbidities risk optimisation*

Of the whole cohort, 183 (30.3%) were optimally treated for comorbidities. HT was the most prevalent associated disease (78.1%). Treatment regimens and the prevalence of concomitant diseases are summarised in Table S2.

3.4 | ABC compliance and clinical outcomes

After adjusting for clinical variables, we analysed the risk of all-cause mortality and the composite outcome after 6 months and 1 year of follow-up (Table 3). In this time period, 207 composite outcome events occurred, and 87 individuals died.

The mortality rate was significantly lower in ABC group comparing to noncompliant ABC patients (5.8% vs 15.9%, $P = .014$, respectively). A nonsignificant trend was observed in the comparison of the composite outcome rates between ABC and non-ABC groups (25.6% vs 36.8%, $P = .065$, respectively).

In a multivariable regression analysis, the ABC pathway was independently associated with a significantly reduced risk of all-cause death and the composite outcome after 6 months (OR 0.18; 95% CI, 0.42-0.75 and OR 0.54; 95% Cl, 0.30-1.00, respectively) and at 1 year (OR 0.30; 95% Cl, 0.11-0.76 and OR 0.57; 95% Cl, 0.33-0.97, respectively) in comparison to the non-ABC compliant group (Table 3 and Figure 2).

Considering the components of partially fulfilled ABC criteria, there was no statistically significant impact on all-cause mortality and composite outcome after 1 year of follow-up, when only 2 of 3 criteria were met (AB or BC or AC) except for BC compliance, which was associated with lower risk of composite outcome (OR 0.58, 95% Cl, 0.37-0.91) after 1 year (Table 4).

4 | DISCUSSION

This is the first study analysing the compliance of AF management in accordance with the ABC pathway among patients with AF and concomitant DM, based on a real-world observational trial in the Middle East which has a high prevalence of DM. Our study shows that the vast majority of these patients were not managed optimally despite having a high risk of stroke. Second, optimal integrated treatment fulfilling all criteria in the ABC pathway regimen significantly reduced the risk of all-cause mortality and the composite outcome in comparison to the non-ABC compliant group. Third, the lower risk of mortality and composite outcome in ABC

TABLE 1 Baseline characteristics of the study cohort

Characteristics	All patients (n = 603)	ABC group (n = 86)	Non-ABC group (n = 517)	*P* value
Demographics				
Male gender, n (%)	288 (47.8%)	42 (48.8%)	246 (47.6%)	.829
Age, mean ± SD	63.42 ± 11.75	64.8 ± 10.79	63.20 ± 11.92	.253
Weight (kg), mean ± SD	80.69 ± 17.35	83.35 ± 17.96 n = 82	80.25 ± 17.22 n = 495	.135
Height (cm), mean ± SD	163.92 ± 8.94	163.81 ± 9.2 n = 80	163.93 ± 8.90 n = 485	.910
BMI, mean ± SD	30.11 ± 6.30	31.36 ± 7.33 n = 80	29.91 ± 6.10 n = 483	.056
Systolic BP (mm Hg) mean ± SD	134.68 ± 26.20	121.44 ± 13.49	136.89 ± 27.14	<.001
Diastolic BP (mm Hg) mean ± SD	79.91 ± 15.79	72.77 ± 9.85	81.10 ± 16.27	<.001
Comorbidities, n (%)				
Coronary artery disease, n (%)	284 (47.1%) n = 598	48 (55.8%)	236 (46.1%) n = 512	.095
Hypertension, n (%)	490 (81.3%)	69 (80.2%)	421 (81.4%)	.792
Dyslipidemia, n (%)	358 (59.4%) n = 597	63 (73.3%)	295 (57.7%) n = 511	.007
Heart failure, n (%)	202 (33.5%)	28 (32.6%)	174 (33.7%)	.842
Stroke or TIA, n (%)	90 (14.9%)	8 (9.3%)	82 (15.9%)	.114
Peripheral artery disease, n (%)		6 (7.0%)	23 (4.4%)	.310
Sleep Apnoea, n (%)		9 (1.7%)	2 (2.4%) n = 85	.698
Dementia or cognitive defects, n (%)		0 (0%)	28 (5.4%)	.072
Chronic kidney disease n (%)	64 (10.6%)	61 (11.8%)	3 (3.5%)	.021
Stroke or bleeding risk scores				
CHA_2DS_2-VASc, mean ± SD	3.69 ± 1.58	3.60 ± 1.27	3.70 ± 1.63	.604
HAS-BLED, mean ± SD	1.56 ± 1.07	1.38 ± 0.83	1.59 ± 1.1	.096
Echocardiogram				
Left atrium diameter (mm)	43.68 ± 7.94	44.22 ± 7.3 n = 58	43.59 ± 8.03 n = 366	.579
LVEF (%), n = 1490	48.91 ± 14.00	48.93 ± 14.53 n = 60	48.91 ± 13.93 n = 379	.991
Medications, n (%) n = 579, ABC group n = 86, non-ABC group n = 493				
ACEI	256 (42.5%)	58 (67.4%)	198 (40.2%	<.001
ARB	129 (21.4%)	28 (32.6%)	101 (20.5%)	.013
Aspirin	360 (59.7%)	55 (64.0%)	305 (61.9%)	.713
Beta-blocker	338 (56.1%)	62 (72.1%)	276 (56.0%)	.005
Verapamil or Diltiazem	68 (11.3%)	4 (4.7%)	64 (13.0%)	.027
Other calcium channel blocker	79 (13.1%)	6 (7.0%)	73 (14.8%)	.051
Clopidogrel	98 (16.3%)	13 (15.1%)	85 (17.2%)	.628
Diuretics	301 (49.9%)	51 (59.3%)	250 (50.7%)	.141
Digoxin	191 (31.7%)	24 (27.9%)	167 (33.9%)	.277
Statin	423 (70.1%)	83 (96.5%)	340 (69.0%)	<.001
Other lipid-lowering drug	13 (2.2%)	4 (4.7%)	9 (1.8%)	.103
Warfarin	336 (55.7%)	84 (97.7%)	252 (51.1%)	<.001

(Continues)

TABLE 1 (Continued)

Characteristics	All patients (n = 603)	ABC group (n = 86)	Non-ABC group (n = 517)	*P* value
Other anticoagulant	44 (7.3%)	6 (7.0%)	38 (7.7%)	.813
Amiodarone	53 (8.8%)	13 (15.1%)	40 (8.1%)	.038
Flecainide	1 (0.2%)	1 (1.2%)	0 (0%)	.017
Propafenone	8 (1.3%)	0 (0%)	8 (1.6%)	.234
Sotalol	5 (0.8%)	1 (1.2%)	4 (0.8%)	.745

Note: High stroke risk: ♀CHAsDSs-VASc ≥ 2, ♂ CHAsDSs-VASc ≥ 1.

Abbreviations: ACEI, angiotensin-converting-enzyme inhibitors; ARB, angiotensin receptor blockers; BMI, body mass index, LVEF, left ventricular ejection fraction, TIA, transient ischaemic attack.

group was independent of either of the duration of follow up and other adjusted covariables.

Our findings indicate that a low percentage of patients received comprehensive AF treatment, compliant with ABC pathway (14.3%) are consistent with other studies on the subject.[23-25] Stroke prevention and proper AF management are even more important among AF patients with concomitant DM as it increases the risk of death from unfavourable thrombotic events.[26,27] Moreover, AF patients with DM have a high risk of stroke (CHA_2DS_2-VASc ≥ 1), and the age threshold for initiating OAC in an AF patient with DM as his/her only stroke risk factor is 50 years.[28] Hence, anticoagulation should have been implemented to all patients in the DM cohort group, while slightly <50% of them were not prescribed OAC at all. Despite the high risk of stroke associated with AF, only 7%-10% die from stroke.[29,30] The vast majority of deaths are related to cardiovascular complications, especially from heart failure. The ABC pathway underlines the need of proper and holistic symptom control of concomitant diseases and their associated symptoms. This means that not only appropriate anticoagulation, but also optimal management and control of other symptoms and comorbidities lead to reductions in all-cause death and the composite outcome.[29] indeed, AF can be associated with a high mortality despite high overall rates of anticoagulation.[18]

TABLE 2 ABC pathway compliance

Study group	Compliance	Noncompliance
A	349 (57.9%)	254 (42.1%)
B	441 (73.1%)	162 (26%)
C	183 (30.3%)	401 (66.5%)
ABC	86 (14.3%)	517 (85.7%)

Abbreviations: A, anticoagulation, B, symptoms management, C, cardiovascular and other comorbidities treatment.

Our study revealed that only holistic AF management in accordance with all ABC components is related to a reduction in either all-cause mortality or occurrence of the composite outcome. Similarly, Pastori et al[31] showed that the risk of adverse cardiovascular events raised with the number of uncontrolled risk factors. In a clinical trial cohort with adjudicated outcomes, Proietti et al reported progressively lower total risk for all-cause death and composite outcome across the groups with the increasing number of fulfilled ABC components.[23] The same

TABLE 3 Multivariable analyses of all-cause mortality and the composite outcome

	All-cause mortality				Composite outcome			
	6 mo		1 y		6 mo		1 y	
Risk factors	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
AF Type (paroxysmal vs persistent/permanent)	1.28 (0.94-1.75)	.118	1.45 (1.11-1.90)	.007	1.36 (1.10-1.69)	.005	1.36 (1.11-1.65)	.002
Dyslipidemia	1.49 (0.83-2.68)	.187	1.23 (0.75- 2.01)	.413	1.25 (0.83-1.87)	.286	1.08 (0.75- 1.55)	.694
Chronic kidney disease	1.80 (0.87-3.75)	.114	1.73 (0.91-3.31)	.095	1.58 (0.90-1.87)	.114	1.59 (0.93-2.73)	.090
Major bleeding	2.64 (0.89-7.84)	.081	2.71 (1.02-7.22)	.046	2.75 (1.10-6.84)	.030	2.62 (1.04-6.61)	.042
ASA used	0.67 (0.38- 1.18)	.163	0.84 (0.52-1.35)	.469	1.15 (0.78- 1.71)	.483	1.20 (0.84-1.72)	.319
ABC compliance	0.18 (0.04-0.75)	.019	0.29 (0.11-0.76)	.012	0.54 (0.30-1.00)	.049	0.57 (0.33-0.97)	.038

Abbreviations: A, anticoagulation;AF, atrial fibrillation; ASA, acetylsalicylic acid; B, symptoms management; C, cardiovascular and other comorbidities treatment; CI, confidence interval, OR, odds ratio.

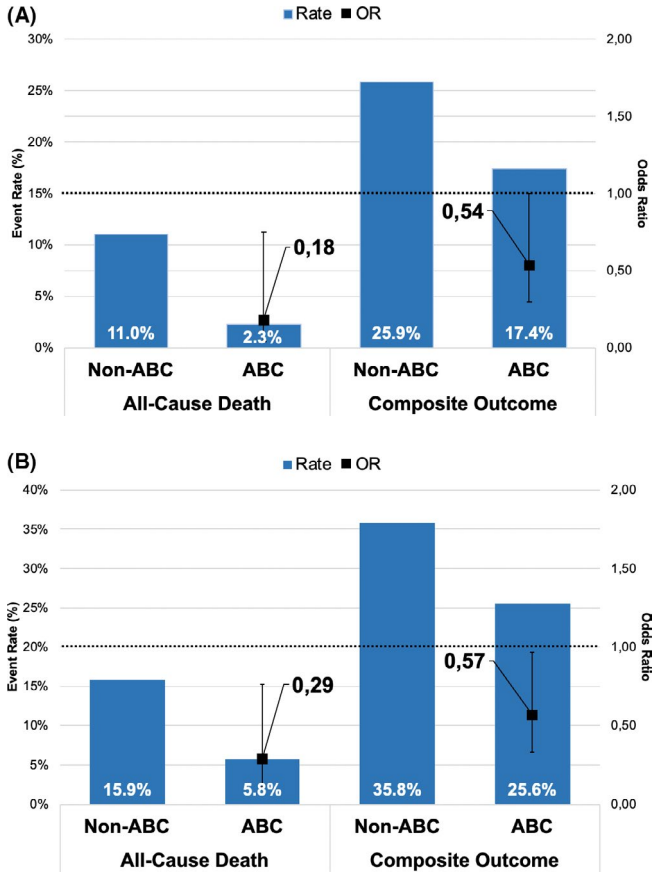

FIGURE 2 Relationship between events rates and odds ratio of clinical outcomes. A, 6-month follow-up. B, 1-year follow-up

trend was presented in a nationwide cohort study based on an Asian population.[25] The above evidence indicates the value of compliance with the ABC pathway for reducing the risk of death and composite adverse outcomes and highlights the importance of integrated, complex care in AF management.[5]

The above findings are essential for any healthcare system as either DM or AF treatment is associated with high healthcare costs. Moreover, DM is, and an independent risk factor for AF development[9,10,32] and their coexistence worsens the outcome among patients.[33-35] Hence, the awareness of the risk factors, early detection of disease and finally, adequate medical care is crucial to reduce cardiovascular mortality in such patients.

4.1 | Strengths and limitations

This is the first study in the Middle East population assessing the compliance of holistic AF management among patients with concomitant DM and the impact on relevant clinical outcomes. The database is based on a large number of consecutive patients from various medical centres who met precisely defined criteria, which enhances the reliability of the analysis results. Nevertheless, there are also some limitations, which should be considered.

This was an observational study with relatively limited of diabetic participants that fulfilled our inclusion criteria for the study, therefore some bias and deficiencies of assessment may have occurred. The compared groups were not homogeneous in terms of concomitant diseases, and some diseases (eg. sleep apnoea) may be undiagnosed. In addition, ABC noncompliant patients were in majority, in keeping with other series.[36] As for DM, its diagnosis, duration and specific type were unknown, which preclude an appropriate evaluation of the impact of DM on the overall cardiovascular risk. In addition, we did not have information about haemoglobin A1c values, which is an indicator of diabetes control in patients with DM. Undeniably, such information would enrich the content of the study and strengthen the credibility of the results. Furthermore, because of the retrospective nature of the study, we were not able to intervene in the treatment regimen that has changed over time, nor do we have data on compliance with drug treatments or therapy cessation, which may have implications for outcomes.[37,37] Although, our registry was conducted in a broad spectrum of clinical settings, in 6 Gulf region countries – but we would be underpowered to perform our analysis by individual country. Due to the retrospective nature of the study, the authors were not able to interfere in the treatment regimen that has changed over time. Finally, the data from the Gulf SAFE registry was collected in 2009-2010, which may affect the reliability of our results in relation to current standards. Nevertheless, although the ABC pathway was not promoted at that time, the general recommendations in accordance with the guidelines for the treatment of AF did not differ from those used in prior treatment approaches.

TABLE 4 Relationship between number of ABC criteria fulfilled and outcomes: all-cause mortality and composite outcome

	All-cause mortality		Composite outcome	
	1 y		1 y	
Number of criteria fulfilled	OR (95% CI)	*P* value	OR (95% CI)	*P* value
AB	0.73 (0.44-1.19)	.206	0.78 (0.54-1.12)	.180
AC	0.72 (0.38-1.36)	.313	1.15 (0.74-1.77)	.538
BC	0.53 (0.28-1.01)	.053	0.58 (0.37-0.91)	.018

Abbreviations: A, anticoagulation; B, symptoms management; C, cardiovascular and other comorbidities treatment; CI, confidence interval; OR, odds ratio.

5 | CONCLUSIONS

Integrated AF care, according to the ABC pathway, was independently associated with a lower risk of all-cause death and the composite outcome, in DM patients with AF. This highlights the importance of a comprehensive and holistic approach to AF management.

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CONFLICT OF INTEREST

None directly related to this paper. GYHL: Consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseon and Daiichi-Sankyo. Speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are directly received personally. Other authors: None declared.

ORCID

Magdalena Domek https://orcid.org/0000-0002-6727-0086
Jakub Gumprecht https://orcid.org/0000-0002-0575-9150
Yan-Guang Li https://orcid.org/0000-0002-9121-1887

REFERENCES

1. Zoni-Berisso M, Lercari F, Carazza T, Domenicucci S. Epidemiology of atrial fibrillation: European perspective. *Clin Epidemiol*. 2014;6:213-220.
2. Charitakis E, Barmano N, Walfridsson U, Walfridsson H. Factors predicting arrhythmia-related symptoms and health-related quality of life in patients referred for radiofrequency ablation of atrial fibrillation. *JACC Clin Electrophysiol*. 2017;3(5):494-502.
3. Gumprecht J, Domek M, Lip GYH, Shantsila A. Invited review: hypertension and atrial fibrillation: epidemiology, pathophysiology, and implications for management. *J Hum Hypertens*. 2019;33:824-836.
4. Lamori JC, Mody SH, Patel AA, et al. Burden of comorbidities among patients with atrial fibrillation. *Ther Adv Cardiovasc Dis*. 2013;7(2):53-62.
5. Lip GYH. The ABC pathway: an integrated approach to improve AF management. *Nat Rev Cardiol*. 2017;14:627-628.
6. Delaney JA, Yin X, Fontes JD, et al. Hospital and clinical care costs associated with atrial fibrillation for Medicare beneficiaries in the Cardiovascular Health Study and the Framingham Heart Study. *SAGE Open Med*. 2018;6:2050312118759444.
7. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation*. 1998;98(10):946-952.
8. International Diabetes Federation. IDF Dibetes Atlas 9th edition 2019. Belgium; 2019. https://www.diabetesatlas.org/en/resources/. Accessed January 20, 2020
9. Benjamin EJ, Levy D, Vaziri SM, D'agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort: the Framingham Heart Study. *JAMA*. 1994;271(11):840-844.
10. Psaty BM, Manolio TA, Kuller LH, et al. Incidence of and risk factors for atrial fibrillation in older adults. *Circulation*. 1997;96(7):2455-2461.
11. Krahn AD, Manfreda J, Tate RB, Mathewson FAL, Cuddy TE. The natural history of atrial fibrillation: incidence, risk factors, and prognosis in the manitoba follow-up study. *Am J Med*. 1995;98(5):476-484.
12. Ruigómez A, Johansson S, Wallander MA, Rodríguez LAG. Incidence of chronic atrial fibrillation in general practice and its treatment pattern. *J Clin Epidemiol*. 2002;55(4):358-363.
13. Frost L, Hune LJ, Vestergaard P. Overweight and obesity as risk factors for atrial fibrillation or flutter: The Danish Diet, Cancer, and Health Study. *Am J Med*. 2005;118(5):489-495.
14. Rosengren A, Hauptman PJ, Lappas G, Olsson L, Wilhelmsen L, Swedberg K. Big men and atrial fibrillation: effects of body size and weight gain on risk of atrial fibrillation in men. *Eur Heart J*. 2009;30(9):1113-1120.
15. Huxley RR, Filion KB, Konety S, Alonso A. Meta-analysis of cohort and case-control studies of type 2 diabetes mellitus and risk of atrial fibrillation. *Am J Cardiol*. 2011;108(1):56-62.
16. Bahtiyar G, Gutterman D, Lebovitz H. Heart failure: a major cardiovascular complication of diabetes mellitus. *Curr Diab Rep*. 2016;16:116.
17. Einarson TR, Acs A, Ludwig C, Panton UH. Prevalence of cardiovascular disease in type 2 diabetes: a systematic literature review of scientific evidence from across the world in 2007–2017. *Cardiovasc Diabetol*. 2018;17:83.
18. Lip GYH, Laroche C, Ioachim PM, et al. Prognosis and treatment of atrial fibrillation patients by European cardiologists: one year follow-up of the EURObservational Research Programme-Atrial Fibrillation General Registry Pilot Phase (EORP-AF Pilot registry). *Eur Heart J*. 2014;35(47):3365-3376.
19. Nieuwlaat R, Olsson SB, Lip GYH, et al. Guideline-adherent antithrombotic treatment is associated with improved outcomes compared with undertreatment in high-risk patients with atrial fibrillation. The Euro Heart Survey on Atrial Fibrillation. *Am Heart J*. 2007;153(6):1006-1012.
20. Hendriks JML, De Wit R, Crijns HJGM, et al. Nurse-led care vs. usual care for patients with atrial fibrillation: results of a randomized trial of integrated chronic care vs. routine clinical care in ambulatory patients with atrial fibrillation. *Eur Heart J*. 2012;33(21):2692-2699.
21. Zubaid M, Rashed WA, Alsheikh-Ali AA, et al. Gulf survey of atrial fibrillation events (Gulf SAFE) design and baseline characteristics of patients with atrial fibrillation in the arab middle East. *Circ Cardiovasc Qual Outcomes*. 2011;4(4):477-482.
22. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J*. 2016;37(38):2893-2962.
23. 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.
24. Pastori D, Farcomeni A, Pignatelli P, Violi F, Lip GY. ABC (Atrial fibrillation Better Care) pathway and healthcare costs in atrial fibrillation: the ATHERO-AF study. *Am J Med*. 2019;132(7):856-861.
25. Yoon M, Yang PS, Jang E, et al. Improved population-based clinical outcomes of patients with atrial fibrillation by compliance

with the simple ABC (atrial fibrillation better care) pathway for integrated care management: a nationwide cohort study. *Thromb Haemost*. 2019;19(10):1695-1703.
26. Kannel WB. Diabetes and cardiovascular disease. The Framingham study. *JAMA*. 1979;241(19):2035-2038.
27. Tuomilehto J, Rastenyté D, Jousilahti P, Sarti C, Vartiainen E. Diabetes mellitus as a risk factor for death from stroke: prospective study of the middle-aged finnish population. *Stroke*. 1996;27(2):210-215.
28. Chao T-F, Lip GYH, Lin Y-J, et al. Age threshold for the use of non-vitamin K antagonist oral anticoagulants for stroke prevention in patients with atrial fibrillation: insights into the optimal assessment of age and incident comorbidities. *Eur Heart J*. 2019;40:1504-1514.
29. Fauchier L, Villejoubert O, Clementy N, et al. Causes of death and influencing factors in patients with atrial fibrillation. *Am J Med*. 2016;129(12):1278-1287.
30. Fauchier L, Samson A, Chaize G, et al. Cause of death in patients with atrial fibrillation admitted to French hospitals in 2012: a nationwide database study. *Open Heart*. 2015;2(1):e000290.
31. 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.
32. Allan V, Honarbakhsh S, Casas J-P, et al. Are cardiovascular risk factors also associated with the incidence of atrial fibrillation? A systematic review and field synopsis of 23 factors in 32 population-based cohorts of 20 million participants. *Thromb Haemost*. 2017;117(5):837-850.
33. Domek M, Li YG, Gumprecht J, et al. One-year all-cause mortality risk among atrial fibrillation patients in Middle East with and without diabetes: The Gulf SAFE registry. *Int J Cardiol*. 2020;302:47-52.
34. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke. *JAMA*. 2001;285(22):2864.
35. Fumagalli S, Said SA, Laroche C, et al. Management and prognosis of atrial fibrillation in diabetic patients: an EORP-AF General Pilot Registry report. *Eur Hear J Cardiovasc Pharmacother*. 2018;4(3):172-179.
36. Kozieł M, Simovic S, Pavlovic N, et al. Management of patients with newly-diagnosed atrial fibrillation: Insights from the BALKAN-AF survey. *IJC Hear Vasc*. 2020;26:100461.
37. Gallego P, Roldan V, Marín F, et al. Cessation of oral anticoagulation in relation to mortality and the risk of thrombotic events in patients with atrial fibrillation. *Thromb Haemost*. 2013;110(6):1189-1198.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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