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ORIGINAL ARTICLE

The neurocognitive effects of atrial fibrillation: benefits of the ABC pathway

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Atrial fibrillation (AF) has a recognized association with not only stroke, but also neurocognitive impairment and both vascular and Alzheimer's dementia. Effective management of AF can reduce the risk of such complications. In this narrative review article, we discuss the pathophysiological links between AF and dementia, as well as the benefits of adherence to the guideline-recommended 'ABC' pathway.

Keywords Atrial fibrillation • Neurocognitive • Neurological • Dementia • Cognition • ABC pathway

Introduction

Atrial fibrillation (AF), the most common cardiac arrhythmia, has a well-established association with stroke. Perhaps less well recognized is the link between AF, cognitive impairment, and dementia.[1–3]

Defining terms such as 'cognitive impairment' and 'dementia' is challenging. As noted in previous meta-analyses, different definitions are often used in studies.[1,2] Cognitive impairment, in particular, may be defined in many ways. Generally, this term refers to a decline in the ability to think, remember, reason, or judge. The point when cognitive impairment becomes dementia is difficult to determine.

The World Health Organization defines dementia as 'a syndrome in which there is deterioration in cognitive function beyond what might be expected from the usual consequences of biological ageing'.[4] There is no single test that can diagnose dementia; the diagnosis relies on evidence of cognitive impairment—using validated cognitive screening tools—along with evidence that this is adversely affecting a person's normal daily functioning. To further complicate this, there are multiple types of dementia, including Alzheimer's, vascular, Lewy body, and others.

Although there is overlap between risk factors for both AF and dementia, AF independently predicts cognitive decline and incident dementia.[5] The risk increases further with advancing age, hypertension, dyslipidaemia, depression, smoking, diabetes, and prior stroke.[6,7]

Dementia has a significant impact on quality of life for both the patient and their loved ones. Additionally, the global healthcare economic impact of dementia is substantial—estimated at over $900 billion US dollars in 2016.[8] Hence, there are multiple reasons to prevent this disease, where possible, by addressing risk factors. In this narrative review article, we will discuss the neurocognitive impact of AF, the effect of treatments—such as anticoagulation and rhythm control—and the impact of the Atrial Fibrillation Better Care (ABC) pathway on such outcomes.

The neurocognitive impact of atrial fibrillation

Whilst the evidence for neurocognitive impairment relating to AF is strong (*Table 1*), the pathophysiological links are complex. Numerous mechanisms have been proposed, including microbleeds, cerebral hypoperfusion, neuroinflammation, genetic predisposition, and microembolism resulting in asymptomatic white matter lesions detected on magnetic resonance imaging (MRI)—so-called silent cerebral lesions (SCLs).[9] SCLs are more often seen in patients with AF, regardless of AF type, compared to those in sinus rhythm; being seen in 22% of patients in studies where computed tomography was deployed, and as many as 40% where MRI was used.[10] The rates are similar in Asian and non-Asian individuals.[11] Cha *et al.* reported a higher risk of symptomatic stroke in those with SCLs compared to those without (5.6% vs. 2.7% per year, $P = 0.022$).[6]

Cerebral microbleeds are also more frequently seen in those with AF compared to those in sinus rhythm. A large meta-analysis found microbleeds in 30.1% of AF patients compared with 26.5% of those without AF.[12] Furthermore, the presence of microbleeds in this analysis was associated with a significant 1.7-fold increased risk of mortality and stroke, although heterogeneity was moderate, and confidence intervals were wide. Another meta-analysis found microbleeds to be associated with an increased risk of intracranial haemorrhage, as well as ischaemic stroke.[13]

Additionally, Barber *et al.* found higher levels of thrombotic biomarkers in those with AF and dementia compared to those with AF without dementia,[14] suggesting that the prothrombotic state associated with AF may not be entirely responsible for neurocognitive impairment. Two studies have also shown that left atrial dysfunction, but not size, correlated significantly with risk of dementia[15] and ischaemic cerebrovascular events.[16] This suggests a link between

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Table 1 Meta-analyses studying the relationship between atrial fibrillation and cognitive decline

Effects of atrial fibrillation on cognition and dementia risk			
Study	**Participants**	**Summary of findings**	**Heterogeneity**
Santangeli *et al.* (2012)[77]	77 668	AF was independently associated with development of dementia (HR 1.42, 95% CI 1.17–1.72; $P < 0.001$)	Moderate
Stefanidis *et al.* (2018)[3]	50 544	AF was significantly associated with cognitive decline and dementia (HR 1.26, 95% CI 1.12–1.43; $P < 0.001$)	Low
Lipnicki *et al.* (2019)[7]	48 522	AF was not independently associated with cognitive decline; however, duration of AF and OAC usage were not available	High
Proietti *et al.* (2019)[17]	56 370	AF was significantly associated with development of Alzheimer's dementia (HR 1.30, 1.01–1.59)	Moderate
Kokkinidis *et al.* (2020)[1]	14 360	In patients with prior stroke, there was an association between AF and cognitive impairment or dementia (OR 2.26, 95% CI 1.61–3.19)	Moderate
Papanastasiou *et al.* (2021)[2]	3549 569	AF was significantly associated with cognitive impairment and dementia (OR 1.54, 95% CI 1.35–1.75; $P < 0.001$)	Moderate
Zuin *et al.* (2021)[78]	3559 349	AF was significantly associated with development of dementia, both in <10 year follow-up (aHR 1.59, 95% CI 1.51–1.67, $P < 0.001$) and longer ≥10 year follow-up (aHR 1.37, 95% CI 1.21–1.55; $P < 0.001$)	High
Koh *et al.* (2022)[12]	2822 974	AF was associated with a significantly increased risk of cognitive impairment (HR 1.39; 95% CI 1.25–1.53; $P < 0.001$)	High
Giannone *et al.* (2022)[23]	~1600 000	AF was associated with an increased risk of early onset dementia (RR 1.50, 95% CI 1.00–2.26) with more pronounced effects at older age	High

AF, atrial fibrillation; aHR, adjusted hazard ratio; CI, confidence interval; HR, hazard ratio; OR, odds ratio; and RR, risk ratio.

AF, dementia, and underlying atrial cardiomyopathy—itself caused by established cardiovascular risk factors.

Logic would dictate that the resultant type of dementia would be vascular; however, there is evidence that Alzheimer's dementia also associates with AF.[2,17] Indeed, the risk of Alzheimer's dementia in those with AF may be increased by up to 30%.[17] Proposed mechanisms include abnormal cerebral blood flow resulting in damage to the blood–brain barrier, hypoperfusion relating to irregular cardiac rhythm, atherosclerosis as a consequence of cerebral adaptation to AF, and consequent amyloid-β plaque deposition.[17–19] Hippocampal atrophy has also been noted in those with AF.[20] Heart rates below 50 b.p.m. or above 90 b.p.m. during AF have been associated with increased risk.[21] The risk increases with CHA_2DS_2VASc score, reflective of the added burden of cardiovascular co-morbidities.[22]

Importantly, the duration of AF has been proposed as a mechanism, with those exposed to AF at a younger age at higher risk of cognitive decline, with potentially earlier onset.[17,23] Such long-term outcomes are not measured in rhythm control trials, and as such, the benefit of early rhythm control may be underappreciated. Furthermore, AF patients with cognitive impairment may have a worse long-term prognosis than those without.[24]

The obvious question, then, is whether or not we can reduce the risk of neurocognitive impairment by treating AF with a combination of anticoagulation, rate or rhythm control, and risk factor modification. These elements make up the guideline-recommended ABC pathway[25] and are discussed in detail below.

A—avoiding stroke with anticoagulation

Anticoagulation to prevent stroke forms the 'A' component of the ABC pathway.[25] It is well known that anticoagulation with either vitamin K antagonists (VKAs) or direct oral anticoagulants (DOACs) reduces the risk of stroke in AF patients. Given the premise that cognitive impairment in AF may, at least in part, relate to microemboli and silent infarctions, anticoagulation should theoretically reduce the number of SCLs and the risk of cognitive decline.

Kühne *et al.* recently described new infarcts on MRI at a 2-year follow-up in 5.5% of AF patients, with a direct association with dementia.[26] Over 85% of these lesions were clinically silent and occurred despite anticoagulation. On multivariable regression, anticoagulation trended towards a reduced risk of new SCLs but did not meet statistical significance. Three meta-analyses have, however, found a significant reduction in cognitive impairment with anticoagulation in AF patients, though heterogeneity was high,[27–29] and prospective studies are needed (*Table 2*). Unfortunately, as mentioned above, cognitive decline and dementia are very long-term outcomes, which makes longitudinal analysis challenging.

Risk reduction may be achieved with either VKAs or DOACs. When utilizing VKAs, higher time in therapeutic range is associated with a lower risk.[27,29,30] There is also evidence of superiority for DOACs over VKAs in this setting,[31–33] including in one meta-analysis [hazard ratio (HR) 0.51, 95% confidence interval (CI) 0.37–0.71; $P < 0.00001$].[27]

In contrast to stroke prevention, oral anticoagulants have not been found to outperform antiplatelets in terms of cognitive decline in the general population.[34,35] Given shared cardiovascular co-morbidities may result in arterial atherosclerosis, cerebral emboli may arise from non-cardiac sites such as the carotid arteries. This is treated with antiplatelets rather than anticoagulants, which may explain this finding. In clinical practice, this is of debatable relevance—AF patients meeting guideline-based recommendations should be anticoagulated for stroke prevention.[25] Antiplatelets, meanwhile, are indicated for secondary prevention in those with established atherosclerotic disease. The effect of these treatments upon incident dementia does not, therefore, necessarily alter management. A reduction in neurocognitive risk,

Table 2 Meta analyses studying the effects of oral anticoagulation on cognitive decline in atrial fibrillation

Effects of anticoagulation on AF-related cognitive impairment and dementia			
Study	**Participants**	**Summary of findings**	**Heterogeneity**
Cheng *et al.* (2018)[27]	471 057	Cognitive impairment in AF was significantly reduced by OAC use (HR 0.71, 95% CI 0.69–0.74; $P < 0.001$)	Low
Mongkhon *et al.* (2019)[29]	452 878	OAC therapy (RR 0.79, 95% CI 0.67–0.93; $P = 0.005$) and higher TTR (RR 0.38, 95% CI 0.22–0.64; $P < 0.001$) reduced the risk of dementia in patients with AF	Moderate to high
Zeng *et al.* (2019)[35]	454 273	OAC was associated with significant reductions in cognitive impairment in patients with AF (RR 0.72, 95% CI 0.69–0.75) but was not superior to antiplatelet therapy (RR 1.01, 95% CI 0.68–1.50)	Low to moderate
Lin *et al.* (2021)[28]	613 920	OAC therapy reduced the risk of dementia in patients with AF (RR 0.72, 95% CI 0.60–0.86, $P < 0.001$)	High

AF, atrial fibrillation; OAC, oral anticoagulation; RR, risk ratio; TTR, time in therapeutic range (for vitamin K antagonists).

however, provides further incentive to ensure appropriate patients are initiated on such therapies.

A further question is whether or not left atrial appendage occlusion (LAAO)—utilized in those who are unsuitable for long-term anticoagulation—can reduce the risk of dementia in a similar fashion. The evidence is sparse, although Mohanty *et al.* studied this in 98 patients assigned to LAAO or OAC[36] following AF ablation. They found that cognitive scores decreased by a small but statistically significant amount in the OAC group and were non-significantly different to baseline in the LAAO group. Given the low patient number and the fact that rhythm control with ablation was performed in all patients, these results should be interpreted with caution, and further studies are needed.

The potential benefit of anticoagulation on cognitive function may be an important factor for patients when deciding if they wish to take such medication. Risk aversion is common, and both patients[37,38] and physicians[39] may under or overestimate stroke and bleeding risk. When faced with the potential to reduce the risk of long-term irreversible cognitive decline, decisions may be swayed in favour of anticoagulation.

Since anticoagulation appears to reduce the risk of neurocognitive impairment via thromboembolic means, the next question is whether restoration of sinus rhythm can reduce the risk via improvement in cerebral blood flow. The clinical studies relating to rhythm control described here are summarized in *Table 3*.

B—better symptom control—rate and rhythm control

The 'B' component of the ABC pathway represents 'Better symptom control'. A major element of this involves a decision on whether to pursue rate or rhythm control. The benefits of each approach remain a subject of debate. Symptomatic benefit is the biggest contributing factor; those with highly symptomatic—ideally paroxysmal—AF clearly benefit most from restoration of sinus rhythm. There is emerging evidence of a potential prognostic benefit to early rhythm control,[40] though further studies are needed. It is also widely accepted that catheter ablation is superior to antiarrhythmic medication in maintaining sinus rhythm, whilst also avoiding the potentially toxic side effects of such drugs.

The question of whether rhythm control reduces dementia risk is complex due to the multifactorial mechanisms underlying neurocognitive decline in AF, as discussed earlier. Not all of these will be altered by restoring sinus rhythm. Equally, dementia may take many years to manifest—longer than most clinical trials can reasonably be funded for—and subclinical cognitive decline may go unnoticed. Furthermore, many studies do not adjust for all factors associated with cognitive decline—in particular, socioeconomic circumstances and mental health.

Despite a limited follow-up duration of around 3 years, one population-based study of over 37 000 patients found that AF catheter ablation was associated with a significantly lower incidence of dementia, as well as heart failure, stroke, and mortality[41]—in fact, those who underwent ablation had similar rates of dementia as a control group without AF. This study was limited by a lack of data around anticoagulation, and the authors noted that anticoagulation adherence may be stronger in the ablation group due to closer follow-up. Other studies have shown that the benefits of rhythm control appear independent of anticoagulation status.[42,43]

An observational, propensity-score matched study with very long follow-up (mean 9 years) found a striking reduction in dementia following ablation vs. AF patients who were not ablated [adjusted hazard ratio (aHR) 0.44, 95% CI 0.25–0.78; $P = 0.005$].[44] Whilst limited by methodological constraints, this adds to the evidence that ablation may be of benefit in improving cognitive outcomes.

A further study even found that AF ablation was associated with an increase in cognitive performance at the 12-month follow-up, compared with controls, who showed a slight decrease.[45] This study should be interpreted with caution, however, due to its small sample size, small effect size, and potential selection bias. In keeping with these findings, patients with recurrent AF despite ablation had no significant cognitive improvement, which is similar to another study where dementia was reduced post-ablation, but there was no benefit where ablation was unsuccessful.[46]

A recent, small, prospective observational study assessed cerebral blood flow following catheter ablation for AF.[47] The authors described significant improvements in blood flow and cerebral perfusion, measured by MRI, in the ablation group compared with the medically treated group. This fits with the evidence described earlier—that AF may result in impaired cerebral blood flow and thus may contribute to neurocognitive risk. Non-paroxysmal AF was a significant predictor of improved cerebral blood flow on multivariate analysis—and specifically in those who did not suffer recurrence of AF—suggesting these patients may stand to gain the most benefit.

Two studies have reported on the effects of electrical cardioversion on cerebral perfusion. Gardarsdottir and colleagues studied 27 patients using MRI, showing improvements in cerebral perfusion and

Table 3 Studies assessing the effects of rhythm control on cognitive decline in atrial fibrillation

Effects of rhythm control on AF-related cognitive impairment and dementia			
Study	**Participants**	**Study type**	**Summary of findings**
AFFIRM[52]	4060	Interventional RCT	Cognitive performance was similar at all timepoints between rhythm and rate control groups.
Bunch *et al.* (2011)[41]	37 908	Retrospective observational	Patients treated with AF catheter ablation had similar rates of dementia to a control group without AF, and significantly lower rates than AF patients who did not undergo ablation.
Damanti *et al.* (2018)[42]	1082	Retrospective observational	Cognitive performance was highest in those who underwent rhythm control for AF compared with rate control or no therapy (rhythm control adjusted OR 0.56 95% CI 0.40–0.79; $P = -0.001$).
Jin *et al.* (2019)[45]	308	Prospective observational	After 12 month follow-up, MoCA score significantly improved in the ablation cohort, even after propensity score matching, but not in the unablated cohort.
Tischer *et al.* (2019)[50]	90	Prospective observational	No difference in prevalence or progression of cognitive impairment was detected between ablation and medically treated groups.
Hsieh *et al.* (2020)[44]	2344	Retrospective observational	Over mean 9 year follow-up, the incidence of dementia was lower in the AF group who received catheter ablation compared with AF without ablation (aHR 0.44; $P = 0.005$).
Kim *et al.* (2020)[46]	194 928	Retrospective observational	Over median 52 month follow-up, ablation for AF was associated with reduced risk of dementia compared with medical therapy (HR 0.73, 95% CI 0.58–0.93).
EAST-AFNET 4 (2020)[40]	2789	Interventional RCT	Early rhythm control (mostly with antiarrhythmic drugs) was not associated with significant cognitive change after median 5 years of follow-up (MoCA score treatment effect −0.14 (95% CI −0.39 to +0.12).
Wang *et al.* (2021)[51]	139	Prospective observational	Cognitive scores were significantly improved in the catheter ablation group (with no difference by ablation modality) compared with medically treated patients.
Kim *et al.* (2022)[54]	41 135	Retrospective observational	Rhythm control was associated with significantly reduced risk of dementia (sHR 0.89, 95% CI 0.82–0.97).
Bodagh *et al.* (2022)[55]	15 886	Meta-analysis	Catheter ablation was associated with a significantly lower risk of dementia compared with medical therapy (HR 0.60, 95% CI 0.42–0.88; $P < 0.05$).

AF, atrial fibrillation; aHR, adjusted hazard ratio; MoCA, Montreal Cognitive Assessment; RCT, randomised controlled trial; and sHR, subdistribution hazard ratio.

grey matter perfusion after successful restoration of sinus rhythm.[48] Saglietto *et al.* utilized near-infrared spectroscopy (NIRS) to analyse beat-to-beat perfusion. The authors found that both microcirculatory hypertensive and hypotensive events were reduced by restoration of sinus rhythm.[49] This fits with the pathophysiological evidence described earlier: Although not conclusively proven, a logical hypothesis is that abnormal cerebral blood flow results in microbleeds and infarcts due to intermittent micro-hypertensive and micro-hypotensive events, coupled with attempts by the microcirculation to adapt to this constantly changing environment.

Other data comparing ablation to medical therapy are conflicting. One retrospective study found no difference in cognitive measures between those treated with catheter ablation and medical therapy.[50] This study was significantly limited, however, due to underpowering (only 45 patients) and short follow-up (6 months). Furthermore, the drug arm was inappropriately homogenized; this group could be treated with either rate or rhythm control, but no stratification was performed.

Conversely, a prospective study of 139 patients found significant improvements in cognitive scores with catheter ablation compared to medical therapy.[51] Again, this study allowed rate or rhythm control in the drug arm and did not state the proportion taking each.

Two landmark trials—AFFIRM and EAST-AFNET 4—assessed rate vs. rhythm control strategies for AF.[40,52] AFFIRM was performed entirely using drug therapy. EAST-AFNET 4 allowed catheter ablation; however, the vast majority were managed with antiarrhythmics. It is important to note that oral anticoagulation rates were far higher in the more contemporary EAST-AFNET 4 trial than the older AFFIRM trial. Neither trial demonstrated a significant difference in cognitive performance at 3- and 2-year follow-ups, respectively.[40,53]

Conversely, a recent large retrospective study by Kim *et al.* found significantly reduced dementia risk in those managed by rhythm control (mostly with drugs) compared with rate control (sHR 0.86, CI 0.80–0.93).[54] A recently published systematic review found a similar reduction (HR 0.60, CI 0.42–0.88), but noted that there is conflicting evidence and called for more studies.[55]

Interestingly, a study of 358 AF patients found that poor ventricular rate control (defined as <50 b.p.m. or >90 b.p.m.) was associated with dementia.[21] This points to potential confounding in some studies. Simply assigning patients to rate control does not mean that their heart rate was adequately controlled. Equally, medical rhythm control leaves open the possibility of drug toxicity and polypharmacy, which might adversely affect cognition. Pacemaker implant to prevent bradycardia may be of benefit and is recommended by expert consensus.[56]

Table 4 Studies analysing the effects of risk factor modification on cognitive decline in atrial fibrillation

Effects of cardiovascular risk factor management on AF-related cognitive impairment and dementia			
Study	**Participants**	**Study type**	**Summary of findings**
Wändell *et al.* (2018)[70]	12 096	Retrospective observational	Prescription of antihypertensives, alone or in combination, significantly reduced the risk of dementia in those with AF.
Kim *et al.* (2020)[69]	171 228	Retrospective observational	A U-shaped relationship with blood pressure and dementia risk in AF was noted, with a target of 120/80 being optimal for dementia prevention.
Park *et al.* (2022)[64]	199 952	Retrospective observational	Alcohol abstinence, no current smoking and regular exercise were associated with reduced risk of dementia in newly diagnosed AF patients (HR 0.62, 95% CI 0.57–0.68 for all three behaviours vs. none).
Lee *et al.* (2022)[65]	126 252	Retrospective observational	Smoking cessation, compared with continued smoking, was significantly associated with a reduced risk of dementia in newly diagnosed AF patients (aHR 0.83, 95% CI 0.72–0.95).
Jiang *et al.* (2022)[68]	9361	Subgroup analysis of RCT (SPRINT)	Intensive blood pressure control in those with AF was associated with an increased risk of developing dementia (HR 2.22, 95% CI 1.03–4.80; *P* for interaction = 0.009).

It is worth noting that AF catheter ablation itself may cause SCL formation.[57,58] An in-depth discussion is beyond the scope of this review, but suffice it to say that recent studies suggest these ablation-related SCLs mostly resolve and do not cause long-term cognitive impairment.[59]

Overall, the data suggest that rhythm control—particularly with catheter ablation—may improve the risk of neurocognitive decline in patients with AF. However, many of these studies are retrospective, allowing for potential selection bias—for example, those referred for catheter ablation may be healthier than those assigned to drug therapy. Prospective randomized controlled trials would be ideal but may be impossible due to the long-term nature of the outcome measures. The benefits of antiarrhythmic drugs alone are less certain, especially in the long term.

It is important to recognize that a rhythm control strategy may restore sinus rhythm, but this does not address the underlying risk factors, such as hypertension, obesity, diabetes, and sleep apnoea. Resultant atrial cardiomyopathy may impair LA function, and this may remain impaired despite successful rhythm control.[60] Nevertheless, it is plausible that dysregulated blood flow due to AF may play a causative role in cognitive impairment, and restoration of sinus rhythm may therefore reduce the risk.

There appears to be minimal evidence relating to the 'pace-and-ablate' strategy (atrioventricular nodal ablation with pacemaker implantation). One small study did report a significant improvement in brain perfusion and neurocognitive performance utilizing this approach in 17 patients with medication-refractory high ventricular rates.[61]

C—cardiovascular risk modification—the importance of lifestyle

Addressing cardiovascular risk factors, largely through lifestyle modification, comprises the 'C' component of the ABC pathway. The underlying mechanisms relating these conditions to AF are complex, multifactorial, and incompletely understood, but involve a proinflammatory state with resulting endothelial dysfunction and atrial cardiomyopathy.[62]

Managing such risk factors has established benefits in the treatment of AF itself,[63] so improvements in cognition would be logically expected to follow. Indeed, large retrospective studies have found that smoking cessation, alcohol abstinence, and regular exercise significantly reduce risk of dementia in those with AF.[64–66]

Management of hypertension in AF presents a particular challenge. It is recognized that controlling hypertension reduces the risk of developing dementia in the general population.[67] However, there is evidence that aggressive blood pressure management in those with AF may actually increase the risk of dementia.[68] This might relate to the irregular blood flow state created by AF, with antihypertensives resulting in further cerebral hypoperfusion episodes; however, this is speculative. Kim *et al.* found that the risk was 'U-shaped', with an increase or decrease of blood pressure from an optimal target of 120/80 being associated with an increased risk of dementia in those with AF.[69] Interestingly, in this study, vascular dementia increased with increasing blood pressure, but Alzheimer's increased with reducing blood pressure. Prescription of antihypertensives—specifically thiazides, beta-blockers, calcium channel blockers, and renin–angiotensin–aldosterone system blockers—has been shown to decrease the risk of dementia in this population,[70] but clearly, our understanding of this complex patient group requires further study.

Obesity is unfortunately common in the modern world, and a body mass index >30 is associated with an approximately doubled risk of developing AF.[71] Obesity increases the risk of obstructive sleep apnoea (OSA), which itself has a recognized association with multiple cardiovascular risk factors, such as hypertension, type 2 diabetes mellitus, and ischaemic heart disease. Both obesity and OSA further increase the risk of dementia, independently of AF.[72,73] Investigating and managing sleep apnoea—especially with weight loss strategies—may therefore aid in treating AF-related symptoms and reducing the risk of neurocognitive decline.

Table 4 summarizes the evidence for risk factor modification on neurocognitive decline in patients with AF.

Medical therapy cannot replace lifestyle modification. Unfortunately, lifestyle modification is difficult; so many patients are unable to sustain such measures. Nevertheless, we should continue to encourage improvements in lifestyle, even alongside therapies to mitigate the effects of cardiovascular risk factors. This benefit particularly applies to AF in the context of this review; however, it is noteworthy that healthy lifestyle habits are associated with a reduced risk of developing dementia outside of the setting of AF as well.[74,75]

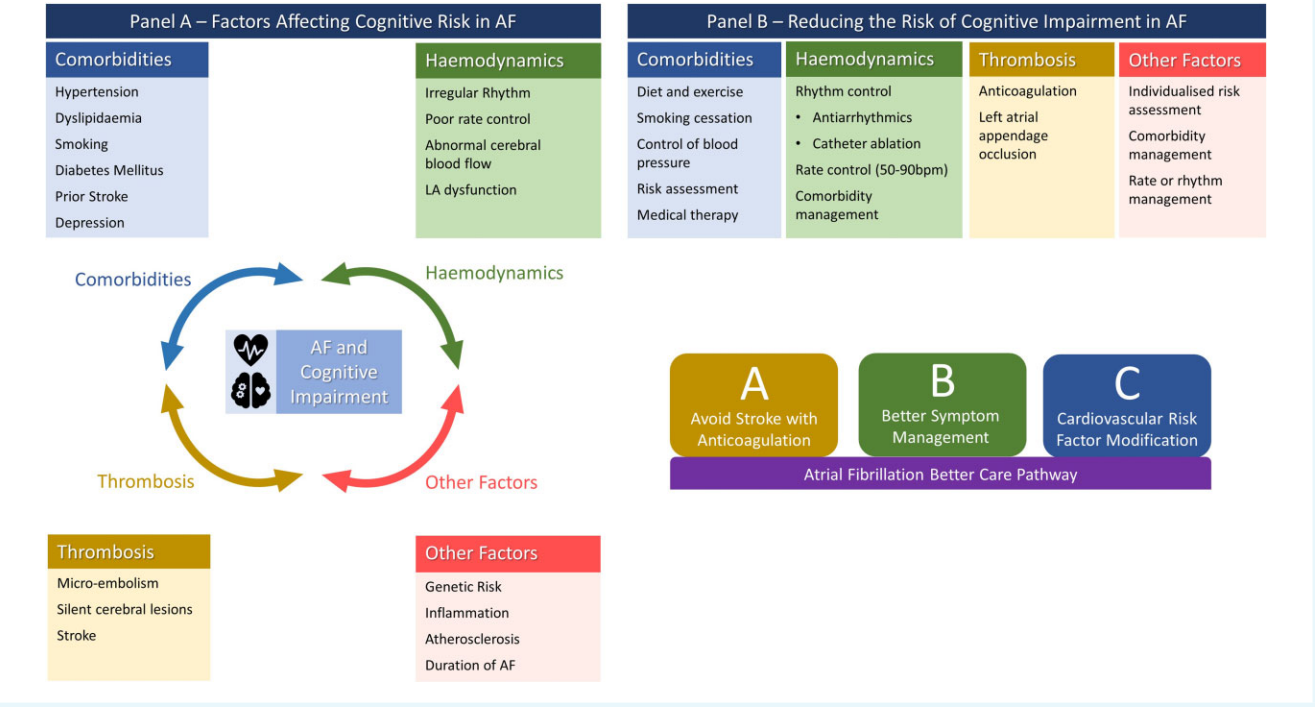

Figure 1 Summary of factors affecting cognitive risk in AF and strategies to reduce the risk. AF, atrial fibrillation; b.p.m., beats per minute; LA, left atrium.

The benefits of adherence to the ABC pathway

The ABC pathway provides a logical framework for the management of AF patients. It follows that, for all the reasons given in the sections above, adherence to the ABC pathway should reduce the risk of neurocognitive impairment amongst AF patients.

This was demonstrated in a study of over 200 000 Korean AF patients.[76] Adherence to the principles of the ABC pathway significantly reduced the incidence of dementia (HR 0.80; 95% CI 0.73–0.87). Though limited by its retrospective nature, this study provides compelling evidence to support regular implementation of the pathway into clinical practice.

A summary of the relationship between AF and cognitive impairment is shown in Figure 1, alongside the benefits of the ABC pathway.

Conclusion

AF is associated with the development of SCLs and microbleeds, and an increased risk of not only stroke, but also vascular and Alzheimer's dementia. The risk of neurocognitive decline in AF patients may be reduced by adherence to the ABC pathway, which is recommended by expert consensus.[56] Specifically, we should ensure that our AF patients are appropriately anticoagulated, have effective rhythm or rate control as appropriate to the individual, and are educated about improving lifestyle to manage cardiovascular risk factors.

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Data availability

No new data were generated as part of this work.

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