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Atrial fibrillation for internists: current practice

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Summary

Atrial fibrillation (AF) has become a global epidemic and puts affected patients at high risk of adverse events. In this review we summarise the current evidence on risk factors and complications of AF, describe current treatment strategies, and outline new fields of research. Current evidence shows that hypertension and obesity are the two most important modifiable risk factors for the development of AF. Patients with AF face an increased stroke risk. Oral anticoagulation reduces this risk substantially. Mainly for reasons of safety and ease of use, non-vitamin K antagonist oral anticoagulants are preferred for stroke prevention. Rate and rhythm control interventions remain important and are mainly used for symptom control in AF patients. Rate control is recommended as an initial treatment and in patients with a low or absent symptom burden. Following the advent of AF ablation 20 years ago, the chances of successful sustained rhythm control have increased. Nevertheless, the procedural risks, although low, must be discussed with the patient in the context of the potential benefits. Heart failure and AF often coexist, which creates a further challenge for optimal AF management. Recent studies have shown that AF patients have a high burden of silent brain lesions, and that these lesions are associated with cognitive dysfunction. A better understanding of these interrelationships may eventually help the development of new prevention and treatment strategies to decrease the burden and complications associated with AF.

Keywords: *atrial fibrillation, risk factors, oral anticoagulation, rate and rhythm control, heart failure, dementia*

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical practice [1, 2], and its prevalence is expected to increase in the near future. AF prevalence correlates strongly with age, with estimates ranging from <1% in individuals aged <60 years to >7% among individuals aged 80 years and older [3]. At age 45, the lifetime risk for developing AF is over 20%. In patients with at least one cardiovascular risk factor, such as hypertension, diabetes or smoking, it is as high as 38% [4]. According to longitudinal data from the Rotterdam Study, the lifetime risk of AF at the age of 55 years was 23.8% in men and 22.2% in women [5]. The fact that men seem to have a higher risk of developing AF than women has been observed for many years [6], but the underlying cause remains unclear. Most established cardiovascular risk factors increase the risk of AF development. Among others, the Women's Health Study showed that hypertension and high body mass index are the strongest potentially modifiable risk factors for incident AF, while the independent contribution of diabetes mellitus seems to be smaller [7–9]. Other known risk factors are a history of coronary heart disease, heart failure and valvular heart disease (predominantly mitral valve stenosis) [10, 11].

The importance of AF as a public health problem is further underscored by its strong and independent association with the risk of stroke, heart failure, death, cognitive dysfunction and a reduced quality of life [11–15]. Stroke and heart failure can be the first manifestations of AF. Patients with established AF have a five-fold increase in their risk of stroke compared to those without arrhythmia [12, 16]. Oral anticoagulation is highly effective at stroke prevention, but residual stroke risk persists in this patient population and current treatment strategies are limited to further reducing this risk. Emerging evidence suggests that patients with AF have a high risk of silent brain lesions, and that these lesions are associated with a decline in cognitive functioning [17].

In this review, we summarise the current evidence on AF risk factors, adverse outcomes in patients with established AF, current treatment strategies, and areas in need of further investigation.

ABBREVIATIONS:

AF	atrial fibrillation
bMRI	brain magnetic resonance imaging
CI	confidence interval
ESC	European Society of Cardiology
MoCA	Montreal Cognitive Assessment
NOAC	non-vitamin K oral anticoagulant
NYHA	New York Heart Association
LA	left atrial
LNCCI	large non-cortical and cortical infarcts
RR	relative risk
SNCI	small non-cortical infarcts
TIA	transient ischaemic attack

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Risk factors and prevention of atrial fibrillation

Hypertension is one of the main potentially modifiable risk factors for AF. Epidemiologic studies have reported that the prevalence of hypertension in AF patients ranges from 49 to 90% [18]. Data from the Women's Health Study suggest that the long-term risk of AF was significantly increased across categories of systolic and diastolic blood pressure, while systolic blood pressure was a better predictor for stroke [7]. Consistent with these observations, data from the Atherosclerosis Risk in Communities (ARIC) Study suggest that elevated blood pressure may be the largest contributor to the overall risk of AF, with an estimated population attributable fraction of 21.6% [19]. The underlying mechanism could include an increase in left ventricular wall thickness or left ventricular stiffness, and the impairment of left ventricular diastolic function associated with hypertension. These processes may cause left atrial (LA) stretch and increase pressure, which leads to remodelling and dilation of the LA, ultimately causing a predisposition to the development of AF [20].

Beyond hypertension, increased body mass index (BMI) and obesity are also key independent risk factors for AF development [8, 21]. Among women free from AF, a total of 18.3% of all new AF cases were attributable to a short-term increase in BMI to >25 kg/m^2 [8]. It has been proposed that obesity and elevated body-fat percentages may lead to ventricular diastolic dysfunction, which may cause LA enlargement and increase susceptibility to atrial remodelling [22]. In addition, studies have shown that elevated body-fat percentages may influence myocardial tissue through increased oxidative stress, which could play a role in the initiation of AF [23].

Heavy alcohol consumption has long been known as a risk factor for AF episodes and has been associated with the so-called "holiday heart syndrome" [24]. Prospective cohort studies have investigated the association of moderate to high alcohol consumption and the risk of developing AF. In the Framingham Heart Study, participants who consumed high amounts of alcohol (>36 g/day) had a significantly higher risk of incident AF [25]. Women who consumed ≥2 drinks/day showed a similarly high risk of developing AF in the future [26]. Meta-analysis showed that the risk of AF increases by 8% with every extra 1 drink/day of alcohol consumed [27]. There seems to be no threshold effect, but more studies are needed at the lower end of the drinking spectrum. Nonetheless, the pathophysiological mechanisms responsible for this association could be that alcohol may promote electrical atrial remodelling, producing an arrhythmogenic substrate and causing myocardial fibrosis within the LA [28, 29]. These electrical and mechanical features may act as triggers for AF.

Regular physical activity and exercise training have favourable effects on cardiovascular risk factors, including improvements in hypertension and diabetes through significant weight loss, and through favourable modifications of cardiac structure and function [30–33]. Given that physical activity lowers the risk factors associated with AF, one may assume that the benefit is also evident as a reduction in AF risk. Several population-based studies have shown that moderate amounts of physical activity significantly reduce AF risk [34, 35], while other studies suggest that high-intensity and endurance exercise are associated with a higher risk of developing AF in young athletes and middle-aged men [36–39]. The increased AF risk in endurance athletes is probably mediated by increased vagal tone, higher volume load during exercise, myocardial damage, and enlargement of the LA [40, 41]. Based on the evidence available and the possible U-shaped relationship of physical activity and incident AF, regular moderate physical activity is recommended to prevent AF, while endurance athletes should be counselled that intense sports can promote AF development [42]. The management of athletes with AF is similar to general treatment regimens of AF patients, with a stronger focus on symptom burden reduction.

Taken together, several modifiable cardiovascular risk factors have been identified as associated with AF risk, and hypertension and obesity explain about 50% of the population attributable risk [19]. This underscores the importance of lifestyle and risk factor management in reducing the AF burden in the general population.

Stroke risk and oral anticoagulation

Stroke

Patients with AF have a high risk of stroke, and epidemiologic evidence suggests that 20-30% of all strokes are due to AF [12, 13, 43–45]. Based on this relationship, several clinically applicable stroke risk-stratification schemes have been developed and validated in AF populations [46–48]. The most widely used one is the CHA_2DS_2-VASc score (congestive heart failure [1 point], hypertension [1 point], age >75 years [2 points], diabetes [1 point], prior stroke, transient ischaemic attack (TIA) or systemic arterial embolism [2 points], vascular disease [1 point], age 65 to 74 years [1 point], female sex [1 point]) [48], which is not only used for stroke risk-stratification, but also aids the decision on whether a patient should receive oral anticoagulation. In general, patients without stroke risk factors do not need antithrombotic therapy, while the great majority of AF patients have stroke risk factors (a CHA_2DS_2-VASc score of 1 or more for men, and 2 or more for women) and would likely benefit from oral anticoagulation.

Oral anticoagulation

Oral anticoagulation effectively reduces stroke risk, by approximately 64% [49, 50]. Vitamin K antagonists (such as phenprocoumon or acenocoumarol) were the oral anticoagulants first used for stroke prevention, and they significantly reduced the risk of stroke in patients with AF [50]. However, the use of vitamin K antagonists is limited by their narrow therapeutic interval, necessitating frequent monitoring and dose adjustments. More recently developed non-vitamin K antagonist oral anticoagulants (NOAC), such as factor Xa inhibitors (apixaban, edoxaban and rivaroxaban) and thrombin inhibitor (dabigatran) have been shown to be at least as effective as vitamin K antagonists for stroke prevention, but safer with regard to adverse events [49]. Clinical trials have showed that NOACs have a lower risk of significant bleeding compared to vitamin K antagonists [49]. This is especially true for intracranial haemorrhage (relative risk [RR] 0.48, 95% confidence interval [CI] 0.39–0.59; p = 0.0001), critical organ bleedings and fatal bleedings. On the other hand, NOAC use is associated with an increase in gastrointestinal bleeding events

(RR 1.25, 95% CI 1.01–1.55; p = 0.04) [49]. Additionally, the practical effect of all NOACs is that there is no need for regular anticoagulation monitoring. Based on this recent evidence, the European Society of Cardiology (ESC) guidelines suggest that when oral anticoagulation is initiated in an AF patient who is eligible for oral anticoagulation, an NOAC (apixaban, dabigatran, edoxaban or rivaroxaban) is preferred to a vitamin K antagonist [42]. Data from Switzerland show that over the last few years, a change in the pattern of oral anticoagulation therapy prescription can be observed, with a shift from vitamin K antagonists to NOACs [51].

Evidence on the use of antiplatelet monotherapy for stroke prevention in AF is very limited [52–54]. Data from randomised trials shows that vitamin K antagonists prevent stroke in AF patients better than single or dual antiplatelet therapy with aspirin or clopidogrel [55]. Antiplatelet therapy increases the risk of bleeding, especially dual antiplatelet therapy, for which the risk is comparable with that for oral anticoagulants [56]. Therefore, antiplatelet therapy cannot be recommended for stroke prevention in AF patients.

Despite the evident benefits of oral anticoagulation, there is still an appreciable residual stroke risk, approximately 1.7% per year for vitamin K antagonists and 1.4% per year for NOACs [49]. Unfortunately, there is currently no evidence available which supports the use of one NOAC over the others, or which supports switching from one NOAC to another in patients who have experienced an ischaemic stroke under NOAC therapy. A retrospective study evaluated the prevalence and management of left atrial thrombi in oral anticoagulated patients who had received a transoesophageal echocardiography prior to pulmonary vein isolation [57]. Among 1358 AF patients, only 11 (0.6%) had a thrombus, while 8 were on oral anticoagulation therapy (5 with NOACs and 3 with vitamin K antagonists). There are currently no guidelines on how to treat these patients with an oral anticoagulant. However, thrombus resolution may be achieved in the majority of patients by changing the anticoagulation regimen, such as switching to vitamin K antagonists or to an NOAC, or a different NOAC. In general, depending on the severity and size of the stroke and the presence of an LA thrombus detected by transoesophageal echography, oral anticoagulation should be reinitiated 3 to 14 days after the event onset, and the decision to restart oral anticoagulation must depend on the risk of recurrent stroke outweighing the risk of secondary haemorrhagic transformation and bleeding [42].

The decision on how to treat AF patients with chronic kidney disease who need NOAC therapy may be challenging, and requires an assessment of renal function using a formula for glomerular filtration rate estimation [58]. The CKD-EPI formula is often used in clinical practice because it is easy, since body weight is not included. However, it should be noted that the large NOAC trials used the Cockcroft-Gault formula, which does incorporate body weight into the calculation of renal function. Dose-adjustments should be performed for dabigatran, rivaroxaban and edoxaban in patients who have a creatinine clearance of <50 ml/min. For apixaban, the dose is reduced in the presence of two or more of the following criteria: age >80 years, weight <60 kg, or a serum creatinine level of >133 µmol/l. For patients with a creatinine clearance <30 ml/min or end stage renal disease, no data are available from randomsed trials, since patients with creatinine clearances of <30 ml/min were excluded in all four major NOAC trials. Nonetheless, in Switzerland and Europe the three factor Xa inhibitors (apixaban, edoxaban, rivaroxaban) are approved to a creatinine clearance of 15ml/min, whereas the cut-off for dabigatran is 30 ml/min (due to its high renal excretion). However, NOACs should generally be used with caution in patients with a creatinine clearance of <30 ml/min.

In general, there is limited evidence on whether AF patients with end-stage renal disease on dialysis benefit from oral anticoagulation. Based on a retrospective analysis, apixaban may be associated with better outcomes compared to vitamin K antagonists [59]. Based on scarce evidence, the US Food and Drug Administration approved apixaban for patients with AF on dialysis, and the drug is used off-label in Switzerland and other countries in dialysis patients.

Gastrointestinal bleedings are a frequent complication in patients treated with oral anticoagulation. Although such bleedings are usually not life-threatening, they should not be underestimated. A focused therapy strategy may be required to treat the cause of bleeding (i.e., gastric ulcer, polyps), but oral anticoagulation should be reinitiated to maintain effective stroke prevention. In situations where patients experience recurrent gastrointestinal bleeding events, an alternative NOAC with a potentially different bleeding risk profile may be considered [60]. Proton-pump inhibitors have been proposed as an option for patients who have a history of gastrointestinal bleeding [61–63]. However, the protective effect has only been evaluated in patients receiving antiplatelet therapy or vitamin K antagonists, and data on the preventive effect in NOAC treated patients are limited.

Implantation of an LA appendage occluder as a mechanical alternative to oral anticoagulation may be considered in selected patients with an absolute contraindication for oral anticoagulation (such as patients with cerebral amyloid angiopathy) and in patients with a history of major bleeding, such as intracranial haemorrhage or gastrointestinal bleeding, who are no longer deemed good candidates for oral anticoagulation [42]. However, the overall weight of evidence for LA appendage occlusion is much lower compared to the evidence on NOACs. Therefore, such treatment decisions should be evaluated in the context of the risks and benefits for the individual patient.

Rate versus rhythm control

Rate and rhythm control interventions, either to improve AF-related symptoms or to restore sinus rhythm, are an integral part of AF management. The decision on which treatment option best fits the individual patient depends on the symptom burden, the patient's expectations and preferences, the duration of AF, and the patient's characteristics.

Rate control

There is little robust evidence available from clinical trials about the best rate control option. Usually, pharmacological rate control can be achieved with beta-blockers, calcium channel blockers (diltiazem, verapamil), and less fre-

quently, digoxin. In the setting of acute new-onset AF, patients should receive rate control interventions using beta-blockers, verapamil or diltiazem [64–66]. Beta-blockers are often the first-line rate-controlling agents [67] because they have better acute heart rate control than calcium channel blockers and digoxin. However, the prognostic benefit of beta-blockers among heart failure patients with reduced ejection fraction is lost in those with AF. An individual, patient-level meta-analysis suggests that beta-blocker therapy leads to a significant reduction in all-cause mortality in heart failure patients with sinus rhythm, but not in patients with AF [68]. Although evidence on the prognostic benefit in heart failure patients with reduced ejection fraction is lacking, the Beta-Blockers in Heart Failure Collaborative Group recommends beta-blockers as a useful first-line rate control agent across all AF patients [69]. This recommendation is mainly based on (1) the good tolerability across patients with sinus rhythm and with AF, (2) the significant functional and symptomatic improvement as a result of beta-blocker administration, and (3) the lack of harm. The use of digoxin may be considered in patients who have concomitant acute systolic heart failure. Verapamil and diltiazem have been shown to improve AF-related symptoms [70]. However, they should not be administered in patients with heart failure because of their negative inotropic effects [66, 71]. Digoxin and digitoxin have been used for rate control for decades, but prescriptions are declining [72]. A randomised trial of heart failure patients showed that digoxin had no mortality benefit compared to placebo, but reduced hospitalisations [73]. Except for critically ill patients, amiodarone should generally not be used for rate-control because of its long-term toxicity. Taken together, the decision on which rate control option best suits a patient should be made on the basis of individual patient characteristics and preferences. Given that all therapies have potential adverse effects, the strategy should be to start at a low dose and then up-titrate until the patient experiences symptom improvements. If pharmacological rate control fails and a patient is not a suitable candidate for rhythm control, a “pace and ablate” strategy (implantation of a permanent pacemaker and ablation of the AV-node) is valuable and has a very high success rate [74–76]. Because it renders patients pacemaker-dependent, it is generally reserved for elderly patients. An additional advantage of this strategy is that patients can stop their rate control medication.

Rhythm control

Sinus rhythm restoration and maintenance is one of the cornerstones of AF management. Rhythm control interventions are indicated in AF patients for symptom improvement and in patients who are haemodynamically comprised. Such interventions consist of antiarrhythmic drug therapy, electrical cardioversion or catheter ablation. Although these interventions have been shown to be beneficial in restoring sinus rhythm, some AF patients may still require repeat procedures or a combination therapy. The choice of whether to initiate antiarrhythmic drug therapy must be carefully evaluated and depends on patient preferences, symptom burden, and potential side-effects of the drugs. In general, flecainide, propafenone, sotalol, or less frequently, dronedarone are recommended for treatment of recurrent symptomatic AF episodes in patients without concomitant heart failure [77–79]. Amiodarone is recommended for treatment of recurrent symptomatic AF episodes in patients with a normal structural heart or with concomitant heart failure [80, 81]. Despite its antiarrhythmic effects, this drug also has proarrhythmic effects such as the occurrence of torsades de pointes, which necessitates regular monitoring of the QT interval in patients on therapy [69]. Long-term therapy with amiodarone is associated with high incidence of extracardiac side effects, including pulmonary toxicity, skin discoloration, thyroid dysfunction, corneal deposits and cutaneous reaction [82, 83]. As a consequence, baseline testing and careful monitoring of patients taking amiodarone is crucial. In the setting of acute new-onset AF, electrical cardioversion is the first-line recommendation in patients presenting with haemodynamic instability [84, 85]. However, antiarrhythmic drugs (such as flecainide, amiodarone or vernakalant) can also restore sinus rhythm in an acute setting and reports suggest that in approximately 50% of patients, sinus rhythm can be successfully restored with pharmacological cardioversion [81, 86, 87]. The advantage of electrical cardioversion is that it restores sinus rhythm much quicker than pharmacological cardioversion. Conversely, pharmacological cardioversion has the advantage that is does not require sedation. In some patients, a single bolus of oral flecainide or propafenone can be self-administrated by the patient, the so-called “pill in the pocket” strategy, to restore sinus rhythm [88]. Electrical cardioversion is associated with an increased risk of stroke in AF patients who are not taking oral anticoagulants [89]. This risk can be significantly reduced by administration of oral anticoagulants for at least three weeks prior to the scheduled cardioversion or by performing transoesophageal echography before cardioversion [90]. The current ESC guidelines recommend that in patients who have been in AF for longer than 48 hours, oral anticoagulation should start at least three weeks before the scheduled cardioversion (or a transoesophageal echography should be performed) [42], suggesting that in patients with AF lasting less than 48 hours, this may not be required [91]. However, a large, multicentre, retrospective cohort study showed that although the general stroke risk is low in patients presenting with AF lasting less than 48 hours, the risk becomes unacceptably high in patients with cardiovascular risk factors [89]. Additionally, it is often challenging to specify whether the patient had AF longer than 48 hours or not. We therefore generally recommend three weeks of oral anticoagulation or performing a transoesophageal echography to exclude the presence of LA thrombus prior to cardioversion in all patients. In general, oral anticoagulation should be continued for four weeks after the procedure in all patients, and afterwards a decision on long-term oral anticoagulation should be based on stroke risk assessment.

Catheter ablation is indicated in patients when antiarrhythmic drugs fail to reduce the symptom burden or to restore sinus rhythm. Catheter ablation is more effective at sinus rhythm restoration than antiarrhythmic drug therapy and may therefore also be offered as first-line therapy, especially in younger patients and patients who do not tolerate or do not wish to take anti-arrhythmic drugs long-term [92–95]. Data suggest that the effectiveness of catheter ablation can also be achieved in patients with persistent or long-standing persistent AF [96]. In general, sinus rhythm

restoration can be achieved in up to 90% of patients with paroxysmal AF, and in around 50 to 80% with persistent AF [97–101]. Whereas AF ablation improves symptoms, there is currently no evidence that catheter ablation prevents cardiovascular events. Although catheter ablation is a procedure with a high safety profile, complications can occur. In experienced centres, approximately 4% of patients experience complications after catheter ablation, but the majority of complications are usually manageable. The most common are vascular access complications (2%), tamponade (1%) and stroke (<1%) [102, 103]. A significant association between AF ablation operator volume (and hospital volume) and adverse outcomes has been reported, and this underscores the actual clinical relevance of referring patients to experienced operators in large centres [103].

It has been debated whether oral anticoagulation can be withdrawn in patients after successful catheter ablation. A small prospective study found that within 1.3 years after ablation, about two-thirds of patients are able to stay off oral anticoagulation [104]. However, because there are no data available from controlled trials, oral anticoagulation following catheter ablation should generally follow anticoagulation recommendations, regardless of the presumed rhythm outcome.

Given the complexity of the different treatment options for AF, including rate and rhythm control interventions, anticoagulation, and co-existing comorbidities such as heart failure, renal failure, etc., close collaboration between internists and cardiologists is warranted.

Comorbidities and consequences of atrial fibrillation

Heart failure

The association between AF and heart failure was described many years ago, with several observational studies reporting a prevalence of AF ranging from 13 to 27% in heart failure populations [105–107]. For instance, data from the Framingham Heart Study suggest that out of 1470 participants who developed either heart failure or new AF during follow-up, over one-fourth (26%) developed both heart failure and AF [11]. The severity of heart failure (usually measured with the New York Heart Association [NYHA] classification) is positively correlated with the prevalence of AF [108].

Although evidence of the association between these two diseases is eminent, the causative relationship between the disorders has not been fully determined. Both diseases share common cardiovascular risk factors, including age, hypertension, diabetes, obesity, valvular heart disease and structural heart disease. Consequently, therapies directed towards risk factors associated with heart failure may be protective for the development of AF as well. Retrospective analyses of randomised trials have demonstrated that angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, β-blockers and eplerenone reduce the risk of developing AF in patients with heart failure [109–112]. Previous investigations have shown that persistent AF episodes can cause tachycardia-induced cardiomyopathy and that the elimination of these arrhythmias reverses the haemodynamic and clinical manifestations associated with heart failure [113–115]. Given this, sinus rhythm restoration may not only reduce the burden of AF, but may also improve the haemodynamic properties of the left ventricle and subsequently reduce heart failure hospitalisations. Indeed, there is evidence from randomised trials that catheter ablation may lower heart failure admission rates in AF patients with concomitant heart failure compared to medical therapy [116–119]. In this context, further refinement to how we approach the treatment of patients with AF and concomitant heart failure remains the subject of future research.

Cognitive dysfunction

Cognitive dysfunction and dementia place an enormous socioeconomic burden on our health care system [120]. Patients with AF have an increased risk of dementia and cognitive decline [14, 17, 121, 122]. A recent meta-analysis of 21 studies demonstrated that the presence of AF was associated with the risk of developing cognitive impairment (RR 1.40, 95% CI 1.19–1.64), and that the risk was even higher in studies that included patients with a history of stroke (RR 2.70, 95% CI 1.82–4.00) [17]. These findings underscore that stroke, which causes structural damage to brain tissue, increases the risk of cognitive decline in patients with AF, but that some of the association seems to be independent of a prior history of overt stroke. An additional factor that might further explain the association between dementia and AF is the higher burden of cardiovascular risk factors in AF patients as compared to individuals without arrhythmia. These cardiovascular risk factors, including hypertension and diabetes, are known to be associated with both AF and dementia [123].

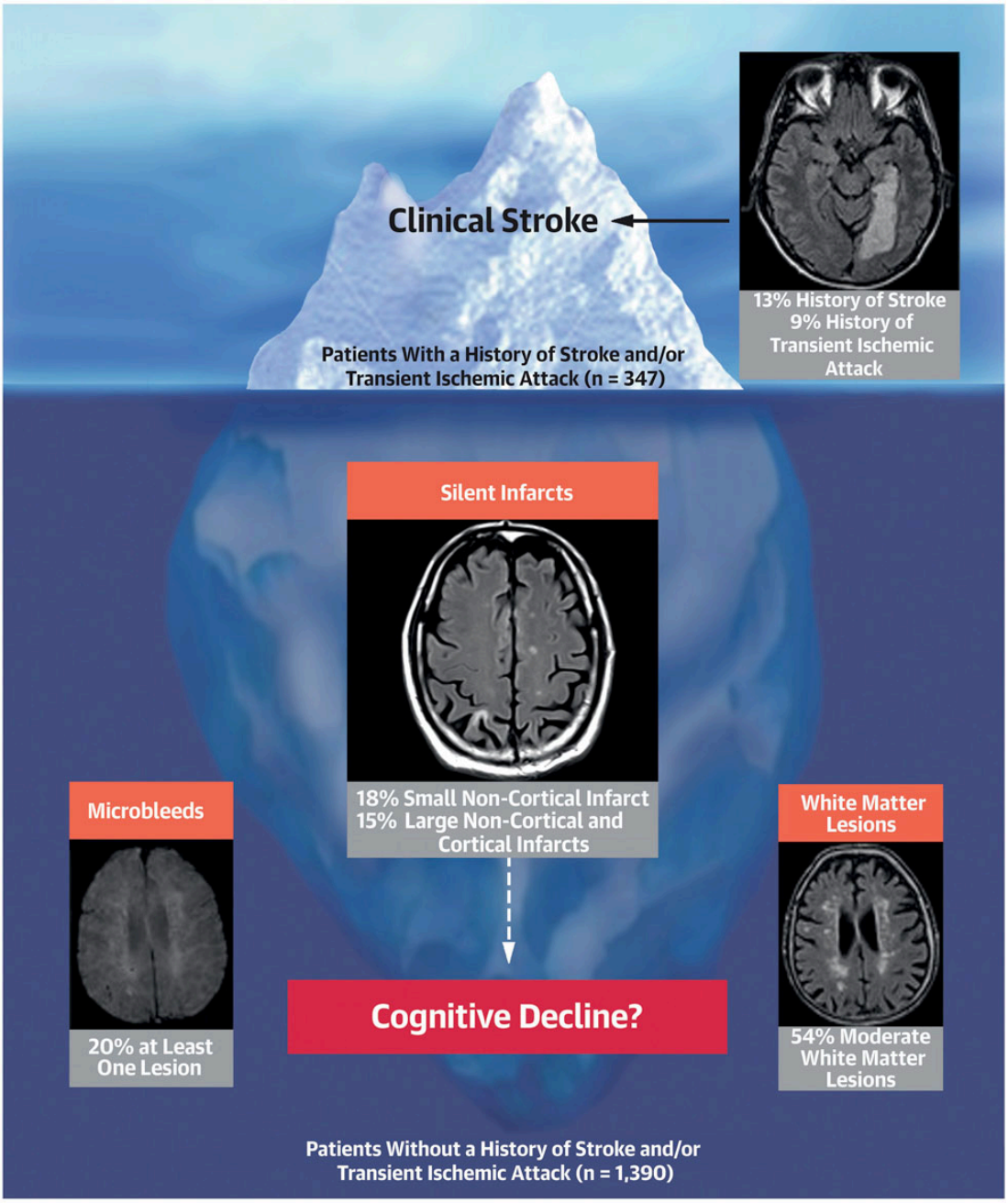
Silent brain lesions can be detected with brain magnetic resonance imaging (bMRI). Up to 20% of individuals from the general population have silent brain infarcts on bMRI [124]. A prospective study performed in individuals free of AF found that the presence of silent brain infarcts on the baseline bMRI was associated with worse performance on neurocognitive tests and a steeper decline in global cognitive function [125]. Also, the presence of silent brain infarcts more than doubled the risk of developing dementia (hazard ratio [HR] 2.26; 95% CI 1.09–4.70). These findings further emphasise that silent infarcts may represent a potential mechanistic correlate of cognitive decline. These relationships have been found in individuals without AF, and there is currently no study that has investigated this association in a high-risk population of AF patients. The Swiss Atrial Fibrillation Cohort (Swiss-AF) Study was designed to investigate the relationship between silent brain lesions and cognitive decline in a large sample of AF patients [126]. Systematic bMRI and cognitive testing using the Montreal Cognitive Assessment (MoCA) were performed in all participants. Cross-sectional analysis revealed that out of 1390 patients without a history of stroke or TIA, 368 (15%) and 387 (18%) had evidence of a previous, silent large non-cortical or cortical infarct (LNCCI) and a small non-cortical infarct (SNCI), respectively (fig. 1) [127]. Importantly, these observations were found in a cohort of patients with a high prevalence of oral anticoagulation (more than 90% on oral anticoagulants) at the time of the bMRI measurements. Patients with silent LNCCI had significantly lower MoCA scores than those with no LNCCI, suggesting a decreased cognitive performance

in patients with silent brain lesions. The magnitude of this difference in cognitive performance was similar in patients who had a history of stroke, a finding which suggests that these lesions may explain at least part of the increased risk of cognitive dysfunction in these patients. Whether routine bMRI scanning and cognitive performance testing should be performed in patients with AF is the subject of current research.

Conclusions

Over the years, significant progress has been made in the field of AF. Hypertension and obesity are the two most important modifiable risk factors for the development of AF, such that lifestyle management and treatment of these risk factors is key for AF prevention. Lowering alcohol consumption and moderate physical activity reduce AF incidence, whereas high endurance sports may increase the risk of incident AF. Stroke risk stratification and oral anticoagulation therapy remain an integral part of AF management, and NOAC therapy is now considered standard of care in patients qualifying for oral anticoagulation. Rate and rhythm control interventions have been shown to reduce the symptoms, and the choice of which treatment best fits the individual patient often depends on the symptom burden, patient characteristics, and patient expectations and preferences. Heart failure remains one of the ma-

Figure 1: Potential relationships between overt and silent brain lesions and cognitive function in patients with atrial fibrillation (Reproduced with the permission of Elsevier from: Conen et al. J Am Coll Cardiol. 2019;73(9):989–99 [127]).



jor comorbidities and complications in AF patients, and their interrelationship needs further evaluation. Patients with AF have an increased risk of cognitive dysfunction, even in the absence of a history of overt stroke or TIA. Further studies are needed to determine the value of routine bMRI screening and testing of cognitive function to improve risk stratification in patients with AF.

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