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Risk-factor modification to prevent recurrent atrial fibrillation after catheter ablation

ABSTRACT

More and more patients with atrial fibrillation are undergoing catheter ablation as a rhythm-control strategy, but the recurrence rate after the procedure is high. A wide array of risk factors contribute to the pathogenesis of atrial fibrillation, including hypertension, diabetes mellitus, dyslipidemia, obesity, obstructive sleep apnea, metabolic dysfunction–associated steatotic liver disease (MASLD), smoking, alcohol consumption, and physical inactivity. This review summarizes the emerging evidence for periablation risk-factor modification to optimize postablation outcomes.

KEY POINTS

- Because we lack sufficient evidence of benefit specifically in patients with atrial fibrillation undergoing catheter ablation, hypertension and diabetes mellitus should be treated according to guidelines in the general population.
- Current guidelines recommend an initial weight-loss goal of 10% in patients with obesity and atrial fibrillation, followed by a target body mass index of less than 25 kg/m^2.
- There is enough evidence to encourage continuous positive airway pressure (CPAP) use in those with atrial fibrillation and obstructive sleep apnea after catheter ablation, and early data suggest that ablation offers little to patients with atrial fibrillation and obstructive sleep apnea not on CPAP.
- Intensive periprocedural MASLD management may be beneficial in reducing recurrence risk after catheter ablation.

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Catheter ablation effectively controls atrial fibrillation, but in up to half of cases the atrial fibrillation comes back. Can this high recurrence rate be lowered by making sure that the risk factors for atrial fibrillation are under optimal control before patients undergo the procedure, and going forward from there?

We think so, although the evidence is scarce. And we think the best approach is to systematically hit all the risk factors simultaneously, in specialized periablation clinics. Here, we review the evidence supporting periprocedural risk-factor modification to reduce atrial fibrillation recurrence after catheter ablation.

SCOPE OF THE PROBLEM

Atrial fibrillation is the most common cardiac arrhythmia worldwide, affecting approximately 33.5 million people.[1] It is associated with significant morbidity and mortality, increasing the risk of systemic thromboembolic disease, heart failure, and sudden cardiac death.

The etiology of atrial fibrillation is multifactorial, with a wide array of risk factors that contribute to its pathogenesis. In recent years, various modifiable comorbidities such as obesity, diabetes mellitus, smoking, and alcohol intake have emerged as key risk factors. They are not only implicated in the onset of atrial fibrillation, but are also associated with worse response to various management approaches to the disease.

Catheter ablation is growing in popularity as a rhythm-control treatment, and is increasingly being offered to patients who have more complex

TABLE 1
Risk factors for atrial fibrillation

Hypertension
Diabetes mellitus
Dyslipidemia
Obesity
Obstructive sleep apnea
Metabolic dysfunction–associated steatotic liver disease
Smoking
Alcohol consumption
Physical inactivity

conditions and comorbidities. The 2023 American College of Cardiology and American Heart Association guidelines[2] give it a class 1 (strong) recommendation, level of evidence A (high-quality):

- To improve symptoms in patients with symptomatic atrial fibrillation in whom antiarrhythmic drugs have been ineffective, contraindicated, not tolerated, or not preferred, and continued rhythm control is desired.
- To improve symptoms and reduce progression to persistent atrial fibrillation in select patients (generally younger with few comorbidities) with symptomatic paroxysmal atrial fibrillation in whom rhythm control is desired.

But here's the problem: although catheter ablation initially works, the atrial fibrillation eventually recurs in 40% to 50% of cases.[3] About 11% of patients need a repeat ablation procedure within 1 year, and many undergo multiple ablations over a number of years.[4]

Fortunately, we should be able to lower this recurrence rate by optimally treating the risk factors for atrial fibrillation (**Table 1**).

HYPERTENSION: MIXED EVIDENCE, BUT USUAL GUIDELINES APPLY

Hypertension accounts for more cases of atrial fibrillation than any other risk factor—up to 20% of all new cases in population-based longitudinal studies.[5] Hypertensive heart disease involves concentric left ventricular hypertrophy and increased stiffness, resulting in chronically elevated left atrial pressures, which drive subsequent left atrial dilation and arrhythmogenesis.[6]

Studies of hypertension and atrial fibrillation

Although many studies have found a near-linear relationship between blood pressure and risk of new-onset atrial fibrillation, the evidence that intensive blood pressure control reduces the risk is equivocal.

SPRINT (the Systolic Blood Pressure Intervention Trial),[7] for example, found no difference in rates of new atrial fibrillation between patients whose blood pressure was treated intensively vs less restrictively.

The relationship between blood pressure control at the time of ablation and the risk of arrhythmia recurrence is equally complex.

Pallisgaard et al,[8] in a Danish nationwide registry, found hypertension to be an independent risk factor for recurrence after ablation.

Santoro et al,[9] in another study in 531 consecutive patients, found the risk of recurrence to be 40.6% in patients with uncontrolled hypertension, 28.1% in those with controlled hypertension, and 25.7% in those with no hypertension. The similar recurrence rates in patients with controlled hypertension vs no hypertension suggest that intensive blood pressure control in the periprocedural period should be beneficial.

The German Ablation Registry,[10] on the other hand, did not find hypertensive patients to be at higher risk of atrial fibrillation recurrence after catheter ablation compared with normotensive patients.

SMAC-AF (Substrate Modification with Aggressive Blood Pressure Control)[11] is the only randomized controlled trial to date investigating the influence of preprocedural blood pressure control on arrhythmia recurrence risk. One hundred eighty-four patients were randomized to either aggressive blood pressure control (target < 120/80 mm Hg) or standard blood pressure control (target < 140/90 mm Hg). At 6 months, the aggressive-treatment group had lower blood pressure than the standard-treatment group. However, the rates of recurrence were nearly identical (61.4% vs 61.2% at a median of 14 months follow-up). Notably, both groups lowered their blood pressure from their baseline levels, so the study may have underestimated the true effect of blood pressure control. Also, most participants had long-standing atrial fibrillation (and thus likely more advanced atrial myopathy), which would predispose them to recurrent rhythm disturbance.

ERADICATE-AF (Evaluate Renal Denervation in Addition to Catheter Ablation to Eliminate Atrial Fibrillation)[12] demonstrated that performing renal denervation at the time of the ablation procedure reduces blood pressure and arrhythmia recurrence risk. Although this randomized controlled trial may seem to show that intensive blood pressure control at the time of catheter ablation is beneficial, the reduction in arrhythmia recurrence was actually independent of the degree of blood pressure improvement. A unifying mechanism may be a reduction in central sympathetic output after renal denervation.

Blood pressure recommendations and questions

Although the evidence of benefit is mixed, most experts agree on the need to optimize periprocedural blood pressure. In a scientific statement, the American Heart Association recommends following the same guidelines in patients with atrial fibrillation as in the general population, as there are not enough data for atrial fibrillation–specific recommendations.[13] They cite the Joint National Committee targets for blood pressure, ie, less than 140/90 mm Hg for people younger than 60 or with diabetes or chronic kidney disease, and less than 150/90 mm Hg for those age 60 and older.

Which drugs to use? There is some evidence that mineralocorticoid receptor antagonists may reduce the risks of new-onset and recurrent atrial fibrillation. A single-center retrospective study found a higher rate of freedom from recurrent atrial fibrillation after ablation in patients receiving eplerenone than in those not receiving it.[14] However, the potential benefit of intensive periablation blood pressure control (particularly with mineralocorticoid receptor antagonists or angiotensin-converting enzyme inhibitors known to induce cardioprotective remodelling) in patients with paroxysmal atrial fibrillation—and thus a lesser degree of atrial myopathy—is yet to be explored.

DIABETES MELLITUS: USUAL GUIDELINES ALSO APPLY

There is a well-described association between diabetes mellitus and new-onset atrial fibrillation. A meta-analysis involving almost 1.7 million patients reported that those with diabetes mellitus had an approximately 40% higher risk of atrial fibrillation than those without it.[15]

Diabetes mellitus induces arrhythmogenesis through a cascade of microvascular ischemia leading to left ventricular diastolic dysfunction, hypertrophy, and eventual left atrial dilation.[16]

Studies of diabetes and atrial fibrillation

Although the association is not linear, there is strong evidence that the worse the diabetes, the greater the risk of atrial fibrillation. Higher hemoglobin A1c levels and longer duration of diabetes are both associated with higher risk of atrial fibrillation, and diabetes may promote progression of atrial fibrillation from paroxysmal to persistent and permanent.[17]

Emerging data suggest that preprocedural glycemic control affects the outcomes of catheter ablation in patients with diabetes.

Donnellan et al,[18] in an analysis of 298 patients with diabetes mellitus undergoing catheter ablation at a single institution, reported that arrhythmia recurred in only 2% of patients who lowered their hemoglobin A1c level by more than 10% before ablation, compared with 91.1% of patients whose hemoglobin A1c level went up before ablation. Moreover, the greater the hemoglobin A1c reduction, the lower the risk of atrial fibrillation recurrence. Limitations of this study include its retrospective design and confounding factors such as differences in patient motivation and compliance with medical therapy.

Wang et al[19] noted a higher rate of recurrent arrhythmias among patients with diabetes mellitus, but found only a nonsignificant trend toward higher risk with worse glycemic control.

Anselmino et al[20] included almost 1,500 patients in a meta-analysis of 15 studies, which revealed that higher baseline hemoglobin A1c was associated with a higher incidence of recurrent atrial fibrillation.

Diabetes recommendations and questions

As with hypertension, the American Heart Association scientific statement[13] recommends managing diabetes according to current general diabetes guidelines, as not enough data exist for atrial fibrillation–specific recommendations. For most adults with diabetes, this would mean a target hemoglobin A1c of less than 7%.

Which drugs to use? Further analysis is required to ascertain whether certain drugs are more efficacious in reducing recurrent arrhythmogenesis.

Pioglitazone and metformin have been associated with lower incidence of atrial fibrillation recurrence in observational studies.[21,22] The researchers hypothesized that the anti-inflammatory and antioxidant properties of these agents dampen arrhythmogenesis; however, these suggested pleiotropic effects (ie, independent of glycemic control) are not proven.

Sodium-glucose cotransporter 2 (SGLT-2) inhibitors hold particular hope as potential adjunct therapy in the periablation period. Post hoc analysis has shown SGLT-2 inhibitors induce protective left atrial structural remodelling and reduce the incidence of atrial fibrillation onset in patients both with and without diabetes, independent of glycemic control.[23] In DECLARE-TIMI 58 (Dapagliflozin Effect on Cardiovascular Events–Thrombolysis in Myocardial Infarction),[24] the SGLT-2 inhibitor dapagliflozin decreased the incidence of reported episodes of atrial fibrillation in patients with diabetes at high risk. Data from randomized controlled trials of SGLT-2 inhibitors in the periablation setting are awaited.

DYSLIPIDEMIA: NO EVIDENT BENEFIT FROM TREATMENT

The association between dyslipidemia and atrial fibrillation risk remains inconclusive. Indeed, some studies

support a paradoxical relationship whereby lower lipid levels are associated with higher risk of new-onset atrial fibrillation.[25] Regarding recurrence rates after ablation, the data are equally mixed, with some studies finding a similar paradoxical association.[26]

Statins have known pleiotropic anti-inflammatory and antioxidant effects, so in theory they might be expected to reduce the risk of recurrence after catheter ablation. However, a meta-analysis of 9 studies found a protective effect in randomized controlled trials but not in retrospective studies or in the analysis as a whole.[27] The largest randomized controlled trial to date found that high-dose atorvastatin therapy did not decrease recurrence risk at 3 months after ablation (when ablation-induced inflammatory responses are known to trigger recurrent arrhythmogenesis) in patients who had no indication for a statin.[28]

OBESITY: WEIGHT LOSS RECOMMENDED

Numerous large epidemiologic studies have solidly shown that the risk of atrial fibrillation increases with weight. The Framingham Heart Study[29] reported a 4% increase in atrial fibrillation risk with each unit (1 kg/m^2) increase in body mass index, which was independent of confounding factors including hypertension and diabetes mellitus. In a continued observational study of women from the Women's Health Study, increasing body mass index was associated with enhanced risk of developing persistent or permanent atrial fibrillation in women who were free of atrial fibrillation at baseline.[30]

Why would this be? Obesity-induced systemic inflammation is thought to disrupt atrial conduction through fibrotic scar tissue deposition.[31] Diastolic dysfunction is common in patients with obesity and contributes to left atrial remodelling. Interestingly, pericardial and epicardial fat may influence atrial fibrillation development through local paracrine mechanisms.[32] These mechanisms ultimately converge on left atrial enlargement with resultant disruption in electrical conductivity. In The Framingham Heart Study,[29] after adjustment for left atrial diameter, obesity was no longer associated with increased risk of atrial fibrillation, suggesting at least part of the proarrhythmogenic burden of obesity is mediated through left atrial dilation.

Studies of obesity and atrial fibrillation

The relationship between weight and outcomes after catheter ablation for atrial fibrillation has been more extensively explored than that of other risk factors. Numerous large observational studies have proven an inverse relationship between weight and freedom from recurrent atrial fibrillation after ablation.[33,34] In a European study involving almost 2,500 patients, the risk of recurrent arrhythmia at 12 months increased with increasing body mass index.[33] Consequently, there has been significant interest in periprocedural weight loss to improve catheter ablation outcomes.

LEGACY (Long-Term Effect of Goal-Directed Weight Management on Atrial Fibrillation Cohort: A 5-Year Follow-Up Study)[35] enrolled 355 patients with body mass index greater than 27 kg/m^2 awaiting catheter ablation who participated in a multidisciplinary weight-reduction program. Weight loss was found to be inversely correlated with atrial fibrillation recurrence; patients who lost 10% or more of their body weight had 6 times greater likelihood of arrhythmia-free survival compared with those who lost less.

SORT-AF (Supervised Obesity Reduction Trial for AF Ablation Patients).[36] Only 1 randomized controlled trial to date has investigated whether weight reduction before catheter ablation alone improves outcomes. The SORT-AF was a multicenter randomized controlled trial in which 133 patients with paroxysmal or persistent atrial fibrillation and body mass index greater than 30 kg/m^2 were randomized to undergo weight reduction or usual care. A statistically significant reduction in body mass index was achieved in the weight-reduction group; however, no significant difference in recurrence rates was evident. Among those with persistent atrial fibrillation after ablation, a reduction in atrial fibrillation burden was noted in the weight-reduction group.

Although this was a well-executed trial with specialized weight-reduction input from endocrinologists, the mean weight reduction achieved in the treatment arm was only 3.9% of initial body weight, and the noncompliance-with-intervention rate at 12 months was 33%.[36] Previous publications report significantly reduced recurrent arrhythmogenesis when more than 10% loss of initial body weight is obtained; it is likely greater weight reduction was necessary to obtain a significant primary outcome.

Obesity recommendations and questions

The American Heart Association scientific statement[13] recommends an initial weight-loss goal of 10% in patients with atrial fibrillation, followed by an eventual target body mass index of less than 25 kg/m^2.

How to lose weight? There are little data regarding which weight-reduction strategy is most effective in the periablation setting, but the American Heart Association recommends a progressive-intensity exercise program in conjunction with a multidisciplinary diet, as used in most studies to date.[36,37]

A single-center observational study reported that preprocedural bariatric surgery reduced atrial fibrillation recurrence risk to that in nonobese patients.[38] The underlying therapeutic mechanism is likely multifactorial, as bariatric surgery was shown to not only decrease weight in this obese cohort, but also significantly reduce blood pressure and hemoglobin A1c. No randomized controlled trial with a sham-controlled arm has been performed.

Glucagon-like peptide-1 agonists such as semaglutide have emerged as highly effective pharmacotherapies for weight loss in both diabetic and nondiabetic cohorts. The SOCRATES-AF (Semaglutide for the Reduction of Arrhythmia Burden in Overweight AF Patients) trial is currently investigating whether semaglutide reduces atrial fibrillation burden in patients with symptomatic paroxysmal and early persistent atrial fibrillation. However, no studies to date have investigated the potential efficacy of glucagon-like peptide-1 agonists as adjunctive therapy in the periprocedural setting for obese patients with atrial fibrillation undergoing catheter ablation. Similar to that of bariatric surgery, any underlying therapeutic benefits are likely to be pleiotropic—extending beyond weight loss alone.

OBSTRUCTIVE SLEEP APNEA: CPAP ENCOURAGED

An association between obstructive sleep apnea and atrial fibrillation is well documented. Although both disorders share multiple risk factors including obesity and hypertension, the relationship is likely causal. Obstructive sleep apnea promotes atrial fibrillation through oxidative stress–induced left atrial remodelling and enhanced sympathetic tone during hypoxemic episodes—both of which combine to drive left atrial enlargement.[39]

Studies of obstructive sleep apnea and atrial fibrillation

Obstructive sleep apnea is strikingly prevalent in patients with atrial fibrillation.

Gami et al,[40] in a seminal study, found that the proportion of patients with obstructive sleep apnea was significantly higher in those with atrial fibrillation than in cardiology patients without atrial fibrillation with similar rates of key comorbidities (49% vs 32%, $P < .0004$).

Conversely, atrial fibrillation is more common in patients with obstructive sleep apnea.

MrOs Sleep (Outcomes of Sleep Disorders in Older Men Study)[41] found that increasing severity of sleep-disordered breathing was associated with a progressive increase in odds of atrial fibrillation and complex ventricular ectopy. However, sleep-disordered breathing includes both obstructive and central sleep apnea. Complex ventricular ectopy was associated most strongly with obstructive sleep apnea, while atrial fibrillation was more strongly associated with central sleep apnea.

Effective management of obstructive sleep apnea with nocturnal continuous positive airway pressure (CPAP) reduces the risk of progression of atrial fibrillation.

ORBIT-AF (Outcomes Registry for Better Informed Treatment of Atrial Fibrillation)[42] found that patients with atrial fibrillation and obstructive sleep apnea on CPAP were less likely to progress to more persistent forms of atrial fibrillation compared with those not on CPAP.

Two studies to date have demonstrated that recurrence rates of atrial fibrillation after catheter ablation are approximately equal in patients with obstructive sleep apnea on CPAP and those without obstructive sleep apnea, and that atrial fibrillation was significantly more likely to recur in patients with obstructive sleep apnea not on CPAP.[43,44]

Naruse et al,[43] in the first study, prospectively recruited 153 Japanese patients. Atrial fibrillation recurred in 22% of those without obstructive sleep apnea, 30% with obstructive sleep apnea on CPAP, and 53% with obstructive sleep apnea but refusing CPAP. On multivariate analysis, CPAP reduced recurrence by roughly 60%.

Fein et al,[44] in the second study, retrospectively examined 62 patients with obstructive sleep apnea after catheter ablation, of whom 32 used CPAP and 30 did not. Compared with a control group without obstructive sleep apnea who underwent catheter ablation, obstructive sleep apnea was associated with increased atrial arrhythmia recurrence. However, as in the Naruse et al[43] study, arrhythmia-free survival at 1 year in the obstructive sleep apnea group using CPAP was similar to that of patients without obstructive sleep apnea (71.9% vs 66.7%). Summarizing the data, the authors suggest that obstructive sleep apnea therapy should be optimized prior to catheter ablation; otherwise, the efficacy of invasive ablation may be lost.

Although the findings were consistent across both studies, limitations preclude making definitive conclusions. Neither are randomized controlled trials, but rather are case-control studies subject to selection bias. Although some major confounders are accounted for, others are not. Patients with obstructive sleep apnea who are not on CPAP may be inherently less compliant with medical therapy or may have less severe disease compared with those using CPAP. No experimental studies investigating the effect of CPAP on obstructive sleep apnea–related atrial fibrillation pathogenesis have been published to date.

Obstructive sleep apnea recommendations

Clinically, there is enough emerging evidence to encourage CPAP use among patients with atrial fibrillation and obstructive sleep apnea after catheter ablation, and early data suggest that catheter ablation offers very little to patients with atrial fibrillation and obstructive sleep apnea not on CPAP. Current guidelines recommend CPAP for these patients.[2] However, randomized data demonstrating benefit on recurrence rates in the periablation setting are currently lacking.

METABOLIC DYSFUNCTION–ASSOCIATED STEATOTIC LIVER DISEASE

Atrial fibrillation shares many risk factors with metabolic dysfunction–associated steatotic liver disease (MASLD, formerly known as nonalcoholic fatty liver disease or NAFLD), including obesity, diabetes mellitus, and metabolic syndrome. Causality has yet to be proven, but multiple mechanisms of arrhythmogenesis have been proposed, including MASLD-induced proinflammatory stress, autonomic dysregulation, and diastolic dysfunction.[45]

Recent evidence suggests that MASLD is associated with increased recurrence risk after catheter ablation.

Donnellan et al,[46] in a case-control study of 89 patients with MASLD and 178 controls, all of whom underwent catheter ablation at Cleveland Clinic, reported that atrial fibrillation recurred more often in those with MASLD. While obstructive sleep apnea was significantly more common in the MASLD group, which could separately affect recurrence risk, the relationship persisted in multivariate models adjusted for obstructive sleep apnea and other potential confounders. Also, recurrence was more likely with worsening MASLD severity as defined by the NAFLD Fibrosis Score. No other publications to date have investigated this relationship; further data are required to support this association.

Few disease-specific therapies exist for MASLD. Existing data mostly support risk-factor modification such as weight loss and tight glycemic control, strategies that are often used in patients with atrial fibrillation regardless of their liver status.

Interestingly, the Donnellan et al[46] study found that postprocedural risk-factor modification reduced atrial fibrillation recurrence. Atrial fibrillation did not recur among any MASLD patient who lost at least 10% of their body weight after ablation, while 91% of patients who gained weight after catheter ablation had recurrent arrhythmia. Similarly, poor glycemic control before the procedure was associated with worse outcomes. All patients whose hemoglobin A1c rose in the 12 months leading up to ablation developed recurrent atrial fibrillation after catheter ablation, compared with only 36% of patients whose hemoglobin A1c fell before ablation.

Although this was only a single-center retrospective study, it suggests intensive periprocedural MASLD management may be beneficial in reducing recurrence risk after catheter ablation. No publications to date have investigated whether an association exists between MASLD-specific pharmacotherapies, such as vitamin E and pioglitazone, and recurrent arrhythmia risk. As proinflammatory oxidative stress is hypothesized to promote atrial fibrillation in MASLD, these antioxidant agents may be beneficial in patients with MASLD undergoing catheter ablation.

SMOKING AND ALCOHOL CONSUMPTION: QUITTING IS RECOMMENDED

Numerous studies demonstrate an increased risk of atrial fibrillation with both smoking and alcohol consumption. The relationship between smoking and new atrial fibrillation is dose-dependent,[47] while epidemiologic studies indicate that alcohol increases the risk only at moderate to high intake levels (defined as > 7 drinks per week).[48] After catheter ablation, multiple retrospective studies have found higher rates of atrial fibrillation recurrence in smokers (34%–43%) than in nonsmokers (14%).[49,50] Similarly, moderate to high levels of alcohol intake have been associated with recurrence after catheter ablation in multiple studies.[51]

Current guidelines therefore recommend smoking cessation treatment and encouragement to abstain from alcohol for all patients with atrial fibrillation.[2]

PHYSICAL INACTIVITY

Cardiorespiratory fitness is inversely correlated with new atrial fibrillation.

CARDIO-FIT (Impact of Cardiorespiratory Fitness on Arrhythmia Recurrence in Obese Individuals With Atrial Fibrillation),[52] in which patients with atrial fibrillation and obesity were offered a tailored exercise program, showed that improvements in cardiorespiratory fitness increased arrhythmia-free survival regardless of the rhythm-control strategy used. In the periablation setting, evidence suggests higher baseline cardiorespiratory fitness is associated with reduced atrial fibrillation recurrence after ablation.[53]

Although the underlying therapeutic mechanism is likely pleomorphic, echocardiography studies have

TABLE 2
Summary of evidence surrounding preablation and postablation risk-factor modification

Risk factor	Before the procedure	After the procedure
Hypertension	Hypertension increases incidence of atrial fibrillation[5] Periprocedural renal denervation reduces blood pressure and atrial fibrillation recurrence[12] Whether aggressive hypertension management before ablation provides additional benefit in preventing atrial fibrillation recurrences is unclear[11]	Hypertension increases postprocedural atrial fibrillation recurrence risk[8] Rates of recurrence in patients with controlled hypertension are similar to those of patients with no hypertension[9]
Diabetes mellitus	Diabetes mellitus increases incidence of atrial fibrillation[15] Periprocedural role of sodium-glucose cotransporter 2 inhibitors is unclear	Hemoglobin A1c control reduces atrial fibrillation recurrence[18]
Obesity	Obesity increases both incidence and severity of atrial fibrillation[29,30] Preprocedural weight management, including bariatric surgery, improves success[33–35,38]	
Obstructive sleep apnea		Continuous positive airway pressure reduces atrial fibrillation recurrence in patients with obstructive sleep apnea[43,44]
Metabolic dysfunction–associated steatotic liver disease	Preprocedural management is beneficial[46] Role of pharmacotherapy is unclear	

shown a correlation between higher cardiorespiratory fitness and reduced left atrial stiffness and improved left atrial systolic function, which may contribute to lower risk of atrial fibrillation recurrence.[54]

ACTIVE-AF (A Lifestyle-Based, Physical Activity Intervention for Patients With Symptomatic Atrial Fibrillation)[55] randomized 120 patients with atrial fibrillation with or without a history of catheter ablation to either a 6-month tailored exercise program or usual care. On Kaplan-Meier survival analysis, there was a clear arrhythmia-free advantage in the exercise group, with 40% in the exercise group vs only 20% in the usual-care group free from atrial fibrillation at 12 months. Additionally, atrial fibrillation symptom severity, measured by questionnaire, was significantly reduced in the exercise group at both 6- and 12-month follow-up.

Although this trial did not involve patients undergoing ablation, it hints at the likely benefit of periprocedural improvements in cardiorespiratory fitness. Randomized controlled trials directly addressing this question are needed.

The evidence on risk-factor modification before ablation and after ablation is summarized in **Table 2**.[5,8,9,11,12,15,18,29,30,33–35,38,43,44,46]

COMPLETE RISK-FACTOR MODIFICATION

Given the interwoven and synergistic nature of risk factors for atrial fibrillation, simultaneous modification of multiple risk factors in the periablation setting is required.

ARREST-AF (Aggressive Risk Factor Reduction Study for Atrial Fibrillation)[56] is the only published study to date to investigate this question. It was a cohort study in which 281 consecutive patients awaiting catheter ablation with body mass index 27 kg/m^2 or higher and at least 1 cardiovascular risk factor were offered risk-factor modification according to American Heart Association and American College of Cardiology guidelines. Addressed risk factors included weight loss, hypertension, glycemic control, dyslipidemia, alcohol intake, and smoking.

The intervention group significantly lowered their weight, blood pressure, hemoglobin A1c, and lipid levels.

Compared with a cohort that did not undergo any risk factor modification, they had a significantly lower rate of arrhythmia recurrence and lower arrhythmia burden and severity (among those in which atrial fibrillation did recur). The rate of single-ablation, arrhythmia-free survival was 32.9% in the risk-factor modification group vs 9.7% in the control group, and arrhythmia-free survival rates after final ablation was 87% in the intervention group vs 17.8% in the control group. Interestingly, the left atrial volume index decreased significantly more in the intervention group than in the control group.

Although limited by selection and observer bias as a nonrandomized study, ARREST-AF[56] offers very promising insight into the potential efficacy of complete risk-factor modification.

AGGRESSIVE OPTIMIZATION IS THE FUTURE

Despite the expanding use of catheter ablation in managing atrial fibrillation, recurrence outcomes remain suboptimal, particularly among patients with comorbidities. The pathogenesis of atrial fibrillation is complex, involving multiple intertwined risk factors that have a synergistic effect on atrial structural remodelling and atrial arrhythmogenesis. Although modification of each individual risk factor is certainly desirable, simultaneous aggressive optimization of multiple risk factors in specialized periablation clinics is the emerging future.

DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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