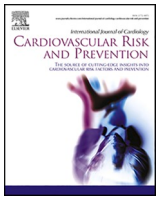
International Journal of Cardiology Cardiovascular Risk and Prevention 23 (2024) 200344

Contents lists available at ScienceDirect

International Journal of Cardiology
Cardiovascular Risk and Prevention

journal homepage: www.journals.elsevier.com/international-journal-of-cardiology-cardiovascular-risk-and-prevention



Impact of lifestyle risk factors on atrial fibrillation: Mechanisms and prevention approaches – A narrative review

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ARTICLE INFO

Handling editor: D Levy

Keywords:
Ablation
Atrial fibrillation
Integrated care
Lifestyle
Risk factor management

ABSTRACT

Both the development and progression of atrial fibrillation (AF) are affected by a range of modifiable lifestyle risk factors. These key modifiable risk factors encompass obesity, hypertension, hypercholesterolemia, diabetes mellitus, smoking, chronic obstructive pulmonary disease, alcohol consumption, exercise, sedentary lifestyle and obstructive sleep apnoea. These lifestyle-dependent factors rarely exist in isolation, but rather exist together, exerting a complex influence on the development of AF. This comprehensive review elucidates the interplay and interdependency of these lifestyle factors in the arrhythmogenesis of AF, by exploring their role in AF substrate formation, modulating properties and triggering mechanisms. We emphasize the importance of targeted prevention strategies by discussing available literature on the effectiveness of treatment strategies targeting multiple risk factors. Additionally, the clinical impacts of integrated care, nurse-led care and mobile health are discussed in the context of lifestyle improvement. These management strategies have favourable applicability in both paroxysmal and persistent AF, and are also beneficial for patients receiving AF ablation. Despite the challenges accompanying lifestyle and prevention strategies, substantial benefits are apparent, such as improved quality of life and better ablation outcomes. This review further emphasizes the essential nature of awareness of appropriate lifestyle modifications as fundamental pillars in the management of individuals with AF.

1. Introduction

Atrial fibrillation (AF) is an epidemic disease that poses an increasing burden on healthcare [1]. Without fundamental improvements in preventive treatment strategies, the projected AF prevalence will have substantial implications for morbidity, mortality, and healthcare costs. Mortality and morbidity can be reduced if rhythm control is applied early following the diagnosis of AF [2]. However, in order to address the growing prevalence of AF, improved preventive strategies are urgently needed.

Both the progression and treatment success of AF are closely linked to a range of modifiable lifestyle risk factors. However, evidence is sparse on whether lifestyle alterations lead to a durable reversal of AF arrhythmogenesis. Previous studies predominantly emphasized the effects of single risk factor interventions, such as sole weight reduction, in a selected population, neglecting the co-incidence and complex interrelatedness of multiple risk factors [11–13].

However, lifestyle risk factors seldomly exist in isolation, complicating AF management and demanding a paradigm shift in how clinicians approach AF. Emerging evidence shows that AF outcomes may improve if multiple risks are simultaneously treated and if health professionals provide integrated care [14–16]. However, as of yet limited evidence is available regarding the interplay of lifestyle factors and how their co-occurrence affects the initiation and progression of AF episodes.

The objective of this article is to comprehensively summarize the interacting effects of risk factors on AF arrhythmogenesis. Furthermore, the effectiveness of integrated risk factor management in AF is evaluated. Additionally, we discuss how combined lifestyle interventions can be applied in the management of AF.

2. Epidemiology and co-incidence of lifestyle risk factors

The lifestyle-related risk factors for the onset of AF have a dose-response effect that increased when combined with other risk factors. We discuss the most relevant risks based on their relative risks (RR) as determined from recent meta-analyses [3–10]. (See Fig. 1 and Table 1).

Each individual element of the metabolic syndrome, encompassing abdominal obesity, hypertension, glucose intolerance and

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https://doi.org/10.1016/j.ijcrp.2024.200344
Received 1 August 2024; Accepted 15 October 2024
Available online 24 October 2024

dyslipidaemia, is correlated with proportionally higher risks of developing AF. Besides, a deterioration of metabolic status is associated AF development [17]. Obesity, defined as a body mass index (BMI) above 30 kg/m^2, increases the risk of AF by 49 % [18]. Any 5 kg/m^2 increase in BMI confers 19–29 % additional risk for developing AF [19]. Likewise, over 20 % percent of AF cases can be attributed to hypertension [20]. This association is more evident for persistent AF than for paroxysmal AF [21]. A further major determinant for AF development is diabetes mellitus, increasing the risk of new AF with 40 %. Diabetics with poor glycaemic control and in longer duration of their condition have an additional risk of developing AF [22]. Additionally, low-density lipoprotein (LDL-)cholesterol and total cholesterol are both associated with increased AF [23].

Obstructive sleep apnoea (OSA) is prevalent in 21–74 % of AF patients [24]. Higher apnoea-hypopnoea severity and frequency lead to a higher AF risk [25]. Both OSA and obesity independently increase the risk of AF. Individuals with both OSA and obesity have a higher risk of developing AF compared to those with only one of these conditions [26,27].

The relationship between AF and physical activity is less straightforward and depends on age and cumulative activity load. Moderate physical activity reduces incident AF compared to inactivy [28,29]. However, vigorous and high-volume endurance activities increase AF risk by over 50 % in athletes under 50 [30]. Middle-aged athletes previously performing endurance training also are at a higher risk of AF [31]. However, in physically active individuals above 65 years do not experience increased AF risk [32].

Further lifestyle related risk factors are alcohol consumption and tobacco smoking. AF risk is increased when consuming more than 3 alcoholic drinks per day [33]. There is a dose-response association per daily drink with 8 % additional risk of AF [34]. Similarly, the risk of AF is higher with increasing smoking pack years [35]. A limitation of alcohol and smoking risk association studies is the reliability of the self-reported data [36].

Table 1
Relative Risk for atrial fibrillation as depicted in Fig. 1.

	Relative Risk for atrial fibrillation	Reference
Chronic Obstructive Pulmonary Disease	2.24 (1.50–3.35)	Xue [3]
Hypertension	1.50 (1.42–1.58)	Aune [4]
Obstructive sleep apnea	1.40 (1.16–1.68)	Ng [5]
Obesity	1.39 (1.30–1.49)	Wu [6]
Current smoking	1.33 (1.14–1.56)	Aune [7]
Diabetes mellitus	1.28 (1.22–1.35)	Aune [8]
Alcohol per 1 drink/day	1.08 (1.06–1.10)	Larsson [9]
Triglycerides	1.02 (0.90–1.17)	Guan [10]

Chronic obstructive pulmonary disease (COPD) confers the highest relative risk among all risk factors for AF [3]. COPD is exposure related and often co-occurs with other risk factors such as hypertension and diabetes and is associated with worse cardiovascular outcomes [37]. The amount of lung function impairment and the presence of exacerbations are both linked with increased AF episodes [38,39].

Several cohort risk studies demonstrated the attributable effects of co-incidental lifestyle risk factors. The Atherosclerosis Risk in Communities study, with a 15-year follow-up, revealed an increased risk of new AF associated with hypertension (HR 1.95), elevated waist circumference (HR 1.40), and impaired fasting glucose (HR 1.16). Importantly, the presence of all these risk factors together substantially elevated the

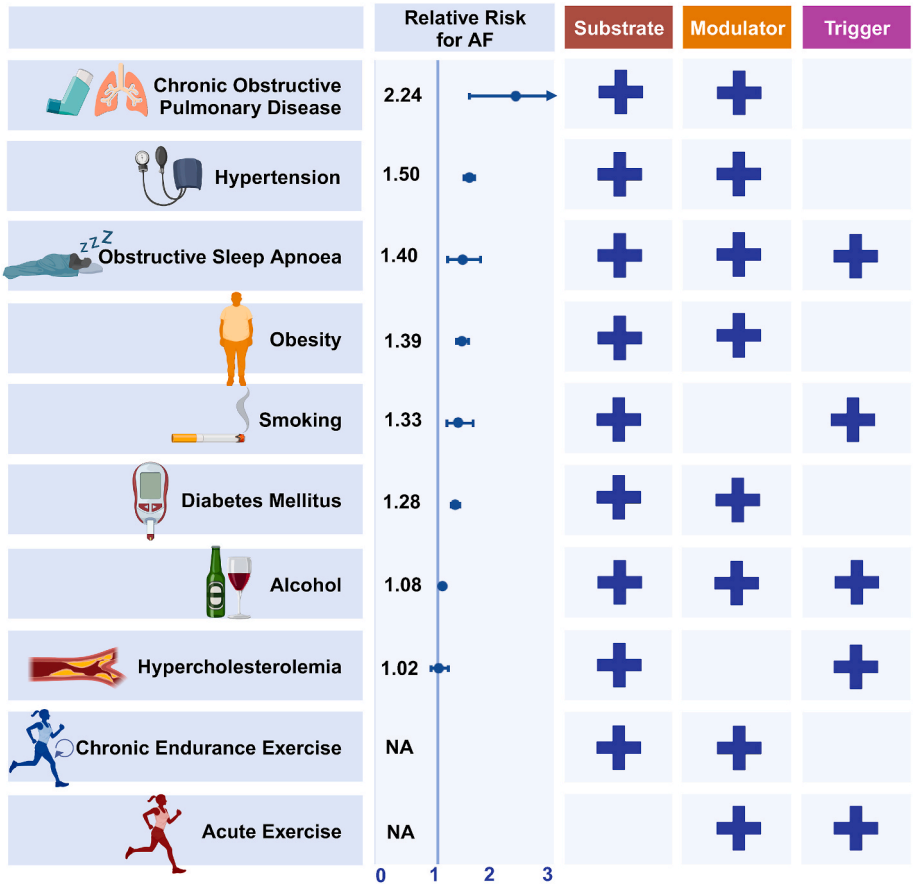

Fig. 1. Modifiable risk factors in the arrhythmogenesis of atrial fibrillation.
AF, atrial fibrillation; NA, not available.

risk of new AF (HR 4.40) [40]. Moreover, in a Swedish cohort with a 17-year follow-up, the combination of smoking, alcohol intake and overweight status was associated with a 2.8-fold difference in AF risk, whereas having only one risk factor let to a 1.3-fold increase [41].

Conversely, the presence of healthy lifestyle factors decreases the risk conferred by other risk factors. Moderate physical activity has a preventive effect on incident AF, particularly in overweight and obese individuals [42,43]. Additionally, in diabetics, alcohol abstinence could lower the incidence of AF [44]. The presence of multiple healthy lifestyle factors is associated with halving the risk of AF [45]. These findings emphasize the importance of addressing multiple lifestyle factors to improve the risk of AF development and progression.

3. Pathophysiology of lifestyle risk factors in atrial fibrillation

3.1. The general progression of atrial fibrillation

Decades ago, Philippe Coumel introduced the classic conceptual model referred to as Coumel's triangle of arrhythmogenesis, to explain the mechanisms underlying the initiation and progression of arrhythmias. According to this model, the three essential components in the pathogenesis of arrhythmias are the substrate, modulating factors and triggers [46]. (Figs. 1 and 2) This concept provides a solid basis for understanding the intricate interplay of various lifestyle risk factors in the arrhythmogenesis of AF.

3.2. Substrate formation

Left atrial remodelling involves a complex interplay of anatomical and electrophysiological changes constituting the atrial substrate. Both atrial dilatation and inflammation are important factors in the remodelling process. As AF progresses from paroxysmal to persistent and permanent forms, substrate becomes increasingly important.

3.2.1. Structural remodelling

3.2.1.1. Atrial dilatation. Atrial dilatation results from various hemodynamic alterations such as increased intracardiac pressure, diastolic dysfunction, ventricular hypertrophy and volume overload [47–50]. These effects are observed in patients with hypertension, diabetes mellitus, alcohol consumption and obesity [50–52]. Hypertension causes chronic pressure overload leading to left ventricular dysfunction and left atrial enlargement [53]. Comparably, both increased body weight and diabetes mellitus are associated with increased left ventricular mass, wall thickness, and diastolic dysfunction [49,52,54,55]. In overweight individuals, alterations in natriuretic peptides and the renin-angiotensin-aldosterone system lead to obesity-associated hypertension [56]. This neurohumoral shift is accompanied by reduced activity of the efferent parasympathetic limb of the baroreflex and impaired atrial M_2-cholinoreceptor, leading to a further increase in blood pressure and further pressure and volume overload of the left atrium [57]. Competitive athletes also exhibit bi-atrial dilatation as a result of the sustained increase in cardiac output during exercise [58]. Compared to patients with low-to-moderate physical activity, patients with high-intensity physical activity demonstrate a greater increase in left atrial volume [59]. Furthermore, among OSA patients, repeat apnoeas and negative tracheal pressures are associated with atrial enlargement, voltage reductions and widespread conduction

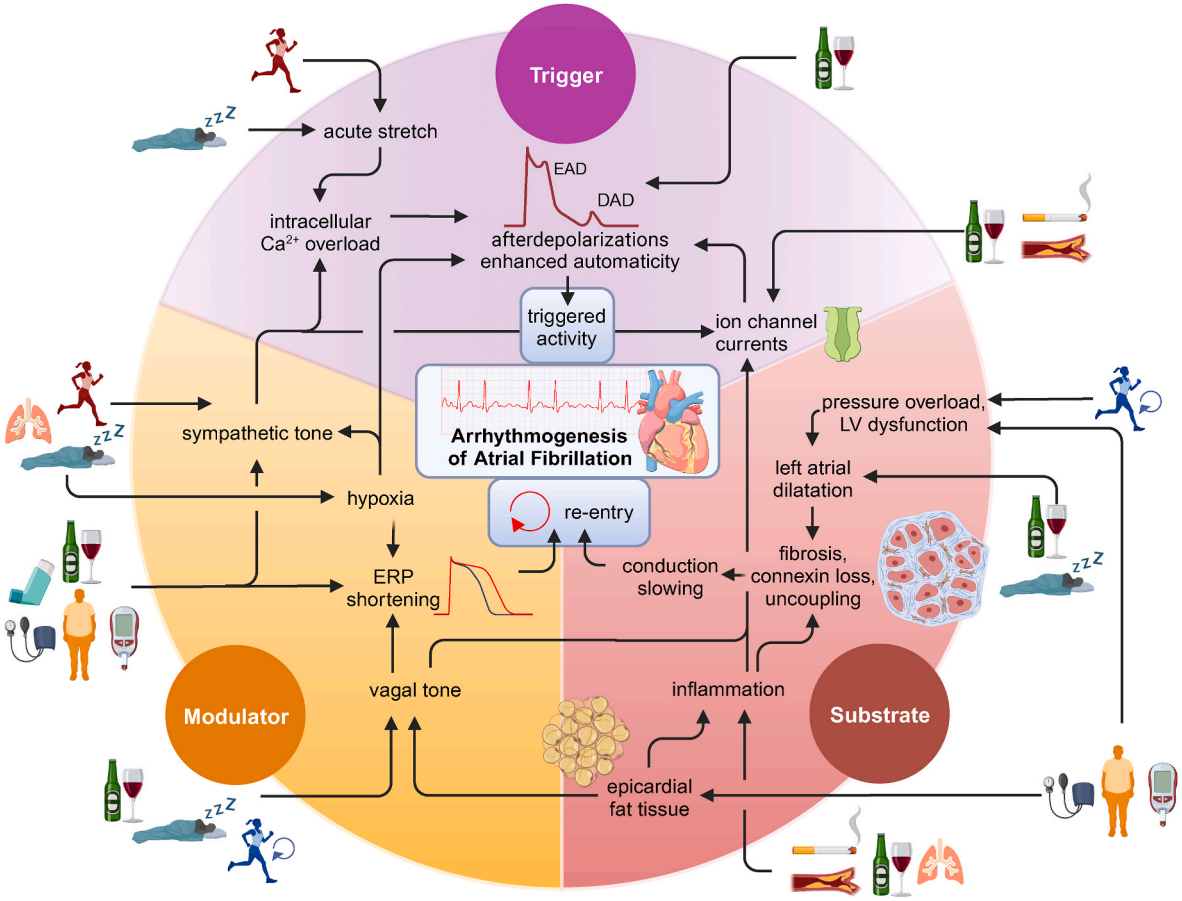

Fig. 2. Interplay of modifiable risk factors in the arrhythmogenesis of atrial fibrillation.
DAD, delayed after depolarization; EAD, early after depolarization; ERP, effective refractory period; LV, left ventricle.

abnormalities [60–67]. Furthermore, COPD is associated with diastolic dysfunction. The right atrium volume might be increased as a result of elevated pulmonary arteria pressure [39]. Lastly, in alcohol consumers, each additional alcoholic drink per day is associated with increasing left atrial dimensions [68].

3.2.1.2. Inflammation and atrial fibrosis. In addition to atrial dilatation, inflammatory processes are essential for substrate formation. An increased epicardial and pericardial fat volume, as often seen in obese patients, leads to increased AF [69]. The increase in pericardial fat leads to inadequate capillarization and a hypoxic state [55]. During hypoxemia, adipocytes promote inflammation by producing adipocytokines and the inflammatory cytokines interleukin-1β, interleukin-6, tumour necrosis factor-α and transforming growth factor β [70,71]. Furthermore, epicardial adipose tissue can partially infiltrate walls of the atria, and thereby cause local inflammation [72]. These inflammatory reactions, oxidative stress and fat infiltrations lead to lipoapoptosis, fibrosis, ion channel dysfunction and ultimately in delay in action potential propagation [48,73,74]. Through this cascade, the presence of pericardial fat results in loss of myocardial function and disturbances in electrical activation and conduction of the atria [75,76]. In patients with hypertension, diabetes, dyslipidaemia or smoking, similar inflammatory processes lead to left atrial alterations. In hypertensive patients, apoptosis and fibrosis are mainly caused by the atrial stretch [77]. In diabetes mellitus, both oxidative stress and inflammatory markers are increased [71]. Alcohol binge drinking is associated with reversible myocardial injury and acute inflammatory reactions, which can lead to AF-triggering [78]. Smoking leads to a combination of oxidative stress, inflammation and thrombosis and profibrotic effects and consequently atrial fibrosis [79].

3.2.2. Electrical remodelling

Atrial dilatation and inflammation eventually result into the electrical remodelling of the atria, forming a re-entry substrate through structural and functional changes, including altered cardiac ion channels. Persistent AF is maintained by the presence of multiple re-entry circuits, facilitated by shortening of the effective refractory period (ERP) and a diminished atrial conduction velocity [80,81]. Shortening of the ERP in the left atrium is seen in diabetic and overweight patients [50,71]. Atrial conduction velocity, determined by connexin proteins between myocytes and cardiofibroblasts, slows with the loss of connexin-43 in patients with hypertension, diabetes, obesity and OSA [71,77,82,83]. In COPD patients, remodelling increases dispersion of P-wave duration, predicting AF onset [39]. Long-term alcohol consumption similarly slows atrial conduction. In animal experiments, alcohol infusion leads to reduced L-type calcium ($I_{Ca,L}$) and sodium (I_{Na}) current density [84]. These membrane potential alterations lead to conduction slowing. Compared to abstainers, alcohol drinkers have an overall lower conduction velocity, leading to a higher risk of AF incidence [85].

3.2.3. Atrial stretch

The AF substrate is further formed by atrial stretch. The immediate consequence of acute atrial stretch is an increase in slow conduction areas, potentially resulting into atrial arrhythmias [86]. This phenomenon is relevant in patient with hypertension and OSA [87]. Stretch in the junction between pulmonary veins and left atrium creates a substrate for re-entry in this region [88]. Direct electrophysiological effects are mediated by stretch-activated ion channels and ligand- and voltage-gated repolarizing potassium channels, that enhance action potential shortening [87].

3.3. Modulating factors

In Coumel's triangle, the degree of interaction between trigger and substrate is determined by modulators.

3.3.1. Autonomic nervous system

The predominant modulator in AF arrhythmogenesis is the autonomic nervous system (ANS). An increase in either adrenergic or vagal activity can contribute to pro-arrhythmic mechanisms [89]. Increased adrenergic activity promotes automaticity and triggered activity based on early and delayed afterdepolarizations. In patients with non-paroxysmal AF, atrial nerve sprouting is increased, resulting in sympathetic hyperinnervation and triggered activity [90]. Conversely, an increase in vagal tone promotes AF by shortening ERP through augmenting the acetylcholine dependent inward potassium current [89].

Being overweight or having a sedentary lifestyle both contribute to autonomic dysfunction, increased sympathetic tone and impaired M_2-cholinoreceptors [91,92]. Obesity-related AF is also promoted through increased parasympathetic nerve activity in the pericardial fat [76]. As long as the increased vagal tone persists, the atria are more susceptible for macro-re-entry and pulmonary veins triggers. Comparable mechanisms play a role in competitive athletes, which have increased vagal tone [58,93].

Alcohol has varying effects on the ANS. Alcohol consumers tend to have a higher heart rate variability than abstainers, indicative for a higher vagal tone [94]. Furthermore, ERP shortening has been demonstrated in the pulmonary veins after alcohol infusion [95]. Individuals susceptible to alcohol-triggered AF are reported to experience AF onset during other vagal-mediated activities, such as meals and rest [96]. However, in young patients prone to alcohol-induced AF, alcohol ingestion was reported to diminish heart rate variability, indicative for exaggerated sympathetic activation [97].

Further autonomic dysregulation occurs in patients with diabetes mellitus, through parasympathetic denervation and heterogenous sympathetic innervation [71]. Similar autonomic dysregulation can result from OSA. During an apnoea, autonomic imbalance is caused by an increased vagal tone due to the activation of the diving reflex, which is followed by a surge in sympathetic tone after the opening of the airway [98]. Hypoxemia stimulates the chemoreceptors in the carotid body, ultimately leading to sympathetic discharges [60]. In COPD patients, the ANS is mainly affected by the respiratory drugs and their adrenergic effects. Short- and long-acting β-agonists decrease the time of atrial refractoriness, making atria more prone to atrial fibrillation [99].

3.3.2. Further modulation

Besides the ANS, hypoxemia itself also acts as modulator in AF arrhytmogenesis [100]. In tissue hypoxia, the accumulation of reactive oxygen species directly shortens the atrial ERP. This effect is relevant in OSA and COPD patients.

3.4. Triggering factors

According to Coumel's triangle, the initiation of AF requires the presence of a trigger that acts on the substrate. About 95 % of AF paroxysms start with atrial premature beats (APBs) [101]. The electrical foci for atrial premature beats are predominantly located in the ostia of the pulmonary veins and may result from ectopic triggered activity, automaticity or re-entry [102]. The myocytes in these structures exhibit distinct electrophysiological characteristics, rendering them more susceptible to initiating premature beats capable of triggering AF episodes.

Lifestyle factors lead to triggers by altering electrical membrane currents and tissue properties. In longstanding persistent AF, APB's originating from non-pulmonary vein regions are more prevalent, especially in patients with metabolic syndrome [103]. Presumably, pericardial fat infiltration promotes ectopic foci, which can trigger AF [76]. Furthermore, cholesterol affects the electrical properties of myocytes by regulating ion channels. High LDL-cholesterol reduces outward potassium currents (I_{Kur}), slowing the early phase of atrial repolarisation

[104]. Comparably, smoking leads to a nicotine-induced elongation of the action potential, by blocking inward potassium currents (I_{k1} and K_{ir}) and reducing outward potassium current (I_{to}) [105,106]. Alcohol upregulates outward potassium currents (I_{to}), shortening atrial ERP around pulmonary veins and causing APBs [84,95]. In OSA, the intrathoracic pressure shifts lead to increased venous return, increased blood pressure, and acute stretch of the left atrium and pulmonary veins, inducing shortening ERP and early afterdepolarizations [87,88,107]. Eventually, the combination of atrial stretch, hypoxia and autonomic activation triggers atrial paroxysms.

4. Treatment of lifestyle risk factors

A reduction in exposure to the various lifestyle risks decreases the potential for AF triggers, modulators and substrate. This could reduce frequency and severity of AF episodes, even in patients with persistent AF and advanced structural substrate [13]. Given the interrelatedness of the lifestyle factors, and the varying impact of sole risk factor reduction, this review summarizes evidence from multiple-risk lifestyle modification studies [108].

4.1. Multiple lifestyle risks treatment and rhythm control

Several studies have been conducted covering a multi-risk treatment in AF. The pioneering trial by Abed et al., revealed that intensive weight reduction by diet and an exercise-plan reduced AF symptom burden and severity [12]. The intervention group lost an average 14 kg compared to 4 kg in the control group, though 69 out of 150 patients were excluded at 15 months, potentially introducing attrition bias. Additional benefits of weight loss included reduced pericardial adipose tissue and ventricular volumes [109]. The observational LEGACY study found that at least 10 % weight reduction combined with lifestyle management prolonged AF-free periods and reduced left atrial size and diastolic dysfunction in overweight patients (mean BMI 33 kg/m^2) [15]. Weight reduction also reversed AF progression towards more persistent forms [110]. The observational CARDIO-FIT trial linked improved cardiorespiratory fitness after lifestyle interventions with longer AF-free periods and reversed cardiac remodelling [111]. Additionally, letting patients undergo their preferred multi-risk treatment for long-term AF freedom was cost-effective [112]. Furthermore, the prospective RACE-3 trial demonstrated that combined therapy, including dietary modifications, physical activity and management of hypertension and hyperlipidaemia, improved rhythm maintenance in patients with persistent AF and heart failure [13]. Additionally, combining hypertension treatment with lipid-lowering therapy improved rhythm maintenance [113,114].

4.2. AF ablation and multi-risk lifestyle modifications

Multifaceted lifestyle modifications have also been studied in the context of improving AF ablation outcomes. The non-randomized AR-REST-AF study revealed that a combination of hypertension treatment, weight loss, glycaemic control, OSA treatment and smoking and alcohol reduction led to better arrhythmia-free survival post-ablation, reduced AF burden, and improved symptoms [14]. In morbidly obese patients (mean BMI 41 kg/m^2), comprehensive risk management, including OSA treatment and weight loss, reduced AF recurrence post-ablation [115]. Even a modest (1.8 %) median weight loss with healthy lifestyle alterations was associated with freedom from AF post-ablation, suggesting that any minor amount of weight loss results in improved ablation outcomes [116]. Conversely, the randomized SORT-AF revealed no difference in AF burden after ablation between a weight reduction group and controls, potentially due to concurrent treatment of apnoea, hypertension and diabetes in controls, and a small median weight loss (5 kg) in the intervention group [117]. Therefore, it is unclear whether there is a lower effect threshold for weight loss. The effect of COPD management in AF ablation candidates remains uncertain. In a prospective pre-ablation cohort, 7 % were diagnosed with COPD, but it is unclear how this affects AF outcomes [118].

4.3. Challenges in the multifaceted risk treatment

Determining the success of lifestyle interventions is not always straightforward and outcomes might be paradoxical. For example, the CHOICE-AF pilot, which explored multi-risk treatment in AF patients, did not result in any weight reduction, yet symptom severity did significantly improve [119]. Likewise, the ALP trial, that studied the effects of exercise and nutrition improvements, showed no improvements in AF burden nor reduction in cardioversions and ablations. Again, quality of life did improve through exercise and nutrition [120].

Furthermore, the durability of lifestyle interventions constitutes a challenge. Most evidence is focused on short-term outcomes. For example, in newly diagnosed AF patients, a rehabilitation program improved quality of life at 6 months, but this effect diminished by 12 months [121]. Despite these negative results, the ongoing PREDIMED Plus trial demonstrates positive long-term effects on biomarkers over 5 years, confirming the feasibility of a sustained intervention [122]. However, the clinical relevance remains to be determined.

Finally, another limitation in lifestyle interventions for AF is that there is no consensus on whether interventions are still effective in advanced AF and obesity. In overweight patients (median BMI 38 kg/m^2) with longstanding persistent AF, a median weight loss of 25 kg did not change ablation outcomes, suggesting that the advanced substrate may reduce the effectiveness of lifestyle interventions [123]. However, Donnellan et al. demonstrated that treatment for OSA, hypertension and weight loss, reduces AF recurrence post-ablation in morbidly obese patients (mean BMI 41 kg/m^2) [115]. Therefore, it is unclear whether all patients could benefit from a multi-risk lifestyle treatment.

4.4. Nurse-led and integrated care

In order to overcome the challenges in risk factor management, AF treatment necessitates a multifaceted approach that encompasses education and interventions targeting the different lifestyle factors and involvement of a multidisciplinary team of healthcare providers. The coordination and integration of various healthcare services and providers to achieve seamless and patient-centred care is referred to as integrated care (Fig. 3). If nurses assume responsibility for the coordination and management of patient care, this is referred to as nurse-led care. The benefits of nurse-led care in AF patients were first

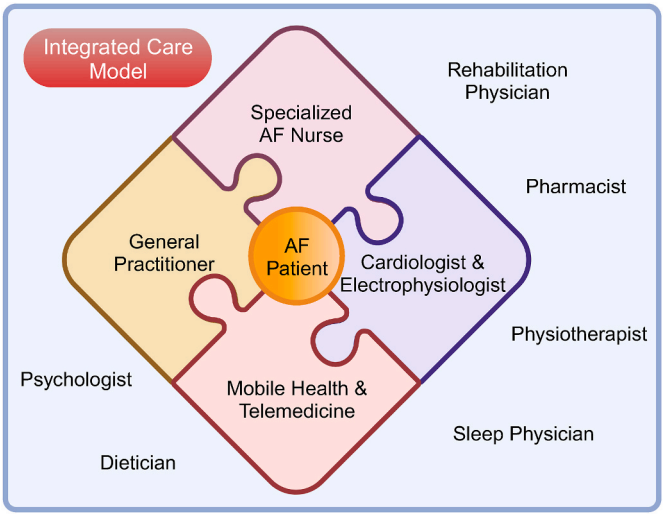

Fig. 3. Integrated care.
AF, atrial fibrillation.

demonstrated in a randomized study by Hendriks et al., showing a reduction in hospitalizations as well as cardiovascular and all-cause mortality compared to usual care (HR 0.65 and 0.44) [124,125]. However, lifestyle modifications were not specifically studied in this trial. The benefits from nurse-led therapy may stem from improved guideline adherence and increased AF-related knowledge of patients, compared to regular care [126,127]. However, the RACE-4 trial did not confirm overall better outcomes with nurse-led care. Patients in centres less experienced with nurse-led care, reported worse outcomes. The specialized AF outpatient clinics that were led by experienced care providers, were more likely to evaluate and address important risk factors such as sleep apnoea, alcohol use, and tobacco use [128,129].

Integrated care spans all clinical stages of AF, from initial diagnosis to post-ablation follow-up. In primary care, integrated care is associated with lower all-cause mortality in AF (RR 0.55) [130]. For patients with permanent AF, nurse-led home-based follow-up prolongs event-free survival, and nurse-led AF clinics reduce readmissions [131,132]. Furthermore, nurse-led education at the time of ablation improves quality of life and symptom severity [133,134]. This accumulating evidence supports the implementation of integrated care in current guidelines [135,136].

4.5. *Lifestyle combined with mHealth*

The combination of mobile health technology (mHealth) with integrated care has emerged as a novel area of research. The use of mHealth allows for a more efficient delivery of education and care, with the potential for improved outcomes. Overall medication adherence can improve when using mobile health [137,138]. The mAFA study, involving over 32,000 patients, demonstrated enhanced patient knowledge, quality of life and readmissions over two years [139]. However, in the mAFA II trial, less robust associations were revealed among patients with multimorbidity, showing the complexity of the effects of mHealth [140]. The optimal integration of mHealth into clinical practice with the objective to improve lifestyle interventions is a current topic of research interest. In a pilot study exploring the effects of multiple risk factor modifications through mHealth and a dedicated nurse, minimal impact on antiarrhythmic drugs use and quality of life were observed [141]. This outcome may be attributed to the modest average weight loss achieved over the 6-month intervention period (1 kg). Similarly, the AF-HEART study showed limited weight loss (3.5 kg at 6 months), but improved quality of life [142]. However, among patients undergoing AF ablation, mHealth did improve compliance with lifestyle changes [143]. Furthermore, the I-STOP-Afib RCT found that mHealth helped patients identify their personal AF triggers and reduce AF events, but without overall improvement in quality of life [144]. These findings underscore the challenges in effectively implementing mHealth interventions in AF management.

5. Discussion

This scoping review highlights the attributable effects of multiple lifestyle risk factors on AF progression and treatment, emphasizing the urgency of a multi-risk approach. While available literature on combined lifestyle modifications and integrated AF care reveals potential benefits, some outcomes are inconsistent. A major determinant in the success of integrated interventions is the amount of weight loss. Furthermore, the efficacy of risk factor modification in non-paroxysmal AF remains a topic of debate. The advanced substrate characterized by left atrial fibrosis is unlikely to reverse. This may explain the findings of the EAST-AFNET4 trial, which demonstrated the superiority of early AF treatment compared to usual care [2]. However, targeting AF triggers and modulating factors in order to slow or stop progression in non-paroxysmal AF, has favourable outcomes reported in trials like RACE-3 [13].

Overall, this review supports comprehensive risk factor management and integrated lifestyle interventions both pre- and post-ablation AF management. By refining the approach for early prevention and long-term management, a substantial proportion of the burden of AF can potentially be prevented. Healthcare providers should overcome challenges such as limited weight loss and aim for durable lifestyle changes. Nevertheless, more research is needed to understand the long-term effects of these interventions on AF management. Efforts should be directed toward optimizing risk factor management clinics and investigating the impact of lifestyle interventions on AF outcomes. Future trials are underway to provide further insights into this urgent topic [145–147].

6. Conclusion

The development and progression of AF is promoted by interacting lifestyle risk factors leading to AF substrate formation, modulators and triggering mechanisms. This review underscores the importance of lifestyle modification as a fundamental pillar for the management of AF. Integrated multiple lifestyle risk factor management has shown promise in improving AF outcomes and quality of life, despite challenges in treatment durability, adherence, and timing. However, evidence from prospective randomized trials remains limited, underscoring the need for further research into the effects of integrated risk factor management on AF.

CRediT authorship contribution statement

Jasper R. Vermeer: Visualization, Writing – original draft, Writing – review & editing. **Johannes L.P.M. van den Broek:** Writing – original draft, Writing – review & editing. **Lukas R.C. Dekker:** Funding acquisition, Supervision, Writing – review & editing.

Acknowledgments

The authors report no relationships that could be construed as a conflict of interest.

This work is supported by the Netherlands Organisation for Health Research and Development (ZonMw) research grant programme 'Top-specialistische Zorg en Onderzoek' (grant number 10070012010001).

References

[1] N.J. Patel, A. Deshmukh, S. Pant, et al., Contemporary trends of hospitalization for atrial fibrillation in the United States, 2000 through 2010 implications for healthcare planning, Circulation 129 (23) (2014) 2371–2379, https://doi.org/10.1161/CIRCULATIONAHA.114.008201.

[2] P. Kirchhof, A.J. Camm, A. Goette, et al., Early rhythm-control therapy in patients with atrial fibrillation, N. Engl. J. Med. 383 (14) (2020) 1305–1316, https://doi.org/10.1056/nejmoa2019422.

[3] Z. Xue, S. Guo, X. Liu, et al., Impact of COPD or asthma on the risk of atrial fibrillation: a systematic review and meta-analysis, Front Cardiovasc Med 9 (2022), https://doi.org/10.3389/fcvm.2022.872446.

[4] D. Aune, Y. Mahamat-Saleh, E. Kobeissi, T. Feng, A.K. Heath, I. Janszky, Blood pressure, hypertension and the risk of atrial fibrillation: a systematic review and meta-analysis of cohort studies, Eur. J. Epidemiol. 38 (2) (2023) 145–178, https://doi.org/10.1007/s10654-022-00914-0.

[5] C.Y. Ng, T. Liu, M. Shehata, S. Stevens, S.S. Chugh, X. Wang, Meta-analysis of obstructive sleep apnea as predictor of atrial fibrillation recurrence after catheter ablation, Am. J. Cardiol. 108 (1) (2011) 47–51, https://doi.org/10.1016/j.amjcard.2011.02.343.

[6] G. Wu, J. Wu, Q. Lu, Y. Cheng, W. Mei, Association between cardiovascular risk factors and atrial fibrillation, Front Cardiovasc Med 10 (2023), https://doi.org/10.3389/fcvm.2023.1110424.

[7] D. Aune, S. Schlesinger, T. Norat, E. Riboli, Tobacco smoking and the risk of atrial fibrillation: a systematic review and meta-analysis of prospective studies, Eur J Prev Cardiol 25 (13) (2018) 1437–1451, https://doi.org/10.1177/2047487318780435.

[8] D. Aune, T. Feng, S. Schlesinger, I. Janszky, T. Norat, E. Riboli, Diabetes mellitus, blood glucose and the risk of atrial fibrillation: a systematic review and meta-analysis of cohort studies, J Diabetes Complications 32 (5) (2018) 501–511, https://doi.org/10.1016/j.jdiacomp.2018.02.004.

[9] S.C. Larsson, N. Drca, A. Wolk, Alcohol Consumption and Risk of Atrial Fibrillation A Prospective Study and Dose-Response Meta-Analysis, 2014.

[10] B. Guan, X. Li, W. Xue, et al., Blood lipid profiles and risk of atrial fibrillation: a systematic review and meta-analysis of cohort studies, J Clin Lipidol 14 (1) (2020) 133–142.e3, https://doi.org/10.1016/j.jacl.2019.12.002.
[11] A. Voskoboinik, J.M. Kalman, A. De Silva, et al., Alcohol abstinence in drinkers with atrial fibrillation, N. Engl. J. Med. 382 (1) (2020) 20–28, https://doi.org/10.1056/nejmoa1817591.
[12] H.S. Abed, G.A. Wittert, D.P. Leong, et al., Effect of weight reduction and cardiometabolic risk factor management on symptom burden and severity in patients with atrial fibrillation, JAMA 310 (19) (2013), https://doi.org/10.1001/jama.2013.280521.
[13] M. Rienstra, A.H. Hobbelt, M. Alings, et al., Targeted therapy of underlying conditions improves sinus rhythm maintenance in patients with persistent atrial fibrillation: results of the RACE 3 trial, Eur. Heart J. 39 (32) (2018) 2987–2996, https://doi.org/10.1093/eurheartj/ehx739.
[14] R.K. Pathak, M.E. Middeldorp, D.H. Lau, et al., Aggressive risk factor reduction study for atrial fibrillation and implications for the outcome of ablation, J. Am. Coll. Cardiol. 64 (21) (2014), https://doi.org/10.1016/j.jacc.2014.09.028.
[15] R.K. Pathak, M.E. Middeldorp, M. Meredith, et al., Long-term effect of goal-directed weight management in an atrial fibrillation cohort, J. Am. Coll. Cardiol. 65 (20) (2015), https://doi.org/10.1016/j.jacc.2015.03.002.
[16] A. Yaeger, N.R. Cash, T. Parham, et al., A nurse-led limited risk factor modification program to address obesity and obstructive sleep apnea in atrial fibrillation patients, J. Am. Heart Assoc. 7 (23) (2018), https://doi.org/10.1161/JAHA.118.010414.
[17] M. Zhao, W. Du, Q. Zhao, et al., Transition of metabolic phenotypes and risk of atrial fibrillation according to BMI: kailuan study, Front Cardiovasc Med 9 (2022), https://doi.org/10.3389/fcvm.2022.888062.
[18] N. Wanahita, F.H. Messerli, S. Bangalore, A.S. Gami, V.K. Somers, J.S. Steinberg, Atrial fibrillation and obesity-results of a meta-analysis, Am. Heart J. 155 (2) (2008) 310–315, https://doi.org/10.1016/j.ahj.2007.10.004.
[19] C.X. Wong, T. Sullivan, M.T. Sun, et al., Obesity and the risk of incident, post-operative, and post-ablation atrial fibrillation, JACC Clin Electrophysiol. 1 (3) (2015) 139–152, https://doi.org/10.1016/j.jacep.2015.04.004.
[20] R.R. Huxley, F.L. Lopez, A.R. Folsom, et al., Absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors: the atherosclerosis risk in communities (ARIC) study, Circulation 123 (14) (2011) 1501–1508, https://doi.org/10.1161/CIRCULATIONAHA.110.009035.
[21] M.C. Thomas, S. Dublin, R.C. Kaplan, et al., Blood pressure control and risk of incident atrial fibrillation, Am. J. Hypertens. 21 (10) (2008) 1111–1116, https://doi.org/10.1038/ajh.2008.248.
[22] S. Dublin, N.L. Glazer, N.L. Smith, et al., Diabetes mellitus, glycemic control, and risk of atrial fibrillation, J. Gen. Intern. Med. 25 (8) (2010) 853–858, https://doi.org/10.1007/s11606-010-1340-y.
[23] H. Watanabe, N. Tanabe, N. Yagihara, T. Watanabe, Y. Aizawa, M. Kodama, Association between lipid profile and risk of atrial fibrillation: niigata preventive medicine study, Circ. J. 75 (12) (2011) 2767–2774, https://doi.org/10.1253/circj.CJ-11-0780.
[24] N.M. Punjabi, The epidemiology of adult obstructive sleep apnea, Proc. Am. Thorac. Soc. 5 (2) (2008) 136–143, https://doi.org/10.1513/pats.200709-155MG.
[25] D. Linz, S. Nattel, J.M. Kalman, P. Sanders, Sleep apnea and atrial fibrillation, Card Electrophysiol Clin. 13 (1) (2021) 87–94, https://doi.org/10.1016/j.ccep.2020.10.003.
[26] A.S. Gami, D.O. Hodge, R.M. Herges, et al., Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation, J. Am. Coll. Cardiol. 49 (5) (2007) 565–571, https://doi.org/10.1016/j.jacc.2006.08.060.
[27] A.S. Gami, D.O. Hodge, R.M. Herges, et al., Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation, J. Am. Coll. Cardiol. 49 (5) (2007) 565–571, https://doi.org/10.1016/j.jacc.2006.08.060.
[28] A.D. Elliott, B. Maatman, M.S. Emery, P. Sanders, The role of exercise in atrial fibrillation prevention and promotion: finding optimal ranges for health, Heart Rhythm 14 (11) (2017) 1713–1720, https://doi.org/10.1016/j.hrthm.2017.07.001.
[29] M.N. Jin, P.S. Yang, C. Song, et al., Physical activity and risk of atrial fibrillation: a nationwide cohort study in general population, Sci. Rep. 9 (1) (2019), https://doi.org/10.1038/s41598-019-49686-w.
[30] A. Aizer, J.M. Gaziano, N.R. Cook, J.E. Manson, J.E. Buring, C.M. Albert, Relation of vigorous exercise to risk of atrial fibrillation, Am. J. Cardiol. 103 (11) (2009) 1572–1577, https://doi.org/10.1016/j.amjcard.2009.01.374.
[31] J. Karjalainen, U.M. Kujala, J. Kaprio, S. Sarna, M. Viitasalo, Lone atrial fibrillation in vigorously exercising middle aged men: case-control study, Br. Med. J. 316 (7147) (1998) 1784–1785, https://doi.org/10.1136/bmj.316.7147.1784.
[32] D. Mozaffarian, C.D. Furberg, B.M. Psaty, D. Siscovick, Physical activity and incidence of atrial fibrillation in older adults the cardiovascular health study, Circulation 118 (8) (2008) 800–807, https://doi.org/10.1161/CIRCULATIONAHA.108.785626.
[33] L. Djoussé, D. Levy, E.J. Benjamin, et al., Long-term alcohol consumption and the risk of atrial fibrillation in the Framingham Study, Am. J. Cardiol. 93 (6) (2004) 710–713, https://doi.org/10.1016/j.amjcard.2003.12.004.
[34] S. Kodama, K. Saito, S. Tanaka, et al., Alcohol consumption and risk of atrial fibrillation: a meta-analysis, J. Am. Coll. Cardiol. 57 (4) (2011) 427–436, https://doi.org/10.1016/j.jacc.2010.08.641.
[35] H. Zuo, O. Nygård, S.E. Vollset, et al., Smoking, plasma cotinine and risk of atrial fibrillation: the Hordaland Health Study, J. Intern. Med. 283 (1) (2018) 73–82, https://doi.org/10.1111/joim.12689.
[36] K.J. Mukamal, B.M. Psaty, P.M. Rautaharju, et al., Alcohol consumption and risk and prognosis of atrial fibrillation among older adults: the Cardiovascular Health Study, Am. Heart J. 153 (2) (2007) 260–266, https://doi.org/10.1016/j.ahj.2006.10.039.
[37] G.F. Romiti, B. Corica, E. Pipitone, et al., Prevalence, management and impact of chronic obstructive pulmonary disease in atrial fibrillation: a systematic review and meta-analysis of 4,200,000 patients, Eur. Heart J. 42 (35) (2021) 3541–3554, https://doi.org/10.1093/eurheartj/ehab453.
[38] L.S.B. Johnson, T. Juhlin, G. Engström, P.M. Nilsson, Reduced forced expiratory volume is associated with increased incidence of atrial fibrillation: the Malmö Preventive Project, Europace 16 (2) (2014) 182–188, https://doi.org/10.1093/europace/eut255.
[39] C.A. Goudis, Chronic obstructive pulmonary disease and atrial fibrillation: an unknown relationship, J. Cardiol. 69 (5) (2017) 699–705, https://doi.org/10.1016/j.jjcc.2016.12.013.
[40] A.M. Chamberlain, S.K. Agarwal, M. Ambrose, A.R. Folsom, E.Z. Soliman, A. Alonso, Metabolic syndrome and incidence of atrial fibrillation among blacks and whites in the Atherosclerosis Risk in Communities (ARIC) Study, Am. Heart J. 159 (5) (2010) 850–856, https://doi.org/10.1016/j.ahj.2010.02.005.
[41] L. Di Benedetto, G. Michels, R. Luben, K.T. Khaw, R. Pfister, Individual and combined impact of lifestyle factors on atrial fibrillation in apparently healthy men and women: the EPIC-Norfolk prospective population study, Eur J Prev Cardiol 25 (13) (2018) 1374–1383, https://doi.org/10.1177/2047487318782379.
[42] L.E. Garnvik, V. Malmo, I. Janszky, U. Wisløff, J.P. Loennechen, B.M. Nes, Physical activity modifies the risk of atrial fibrillation in obese individuals: the HUNT3 study, Eur J Prev Cardiol 25 (15) (2018) 1646–1652, https://doi.org/10.1177/2047487318784365.
[43] F. Azarbal, M.L. Stefanick, E. Salmoirago-Blotcher, et al., Obesity, physical activity, and their interaction in incident atrial fibrillation in postmenopausal women, J. Am. Heart Assoc. 3 (4) (2014), https://doi.org/10.1161/JAHA.114.001127.
[44] Y.J. Choi, K Do Han, E.K. Choi, et al., Alcohol abstinence and the risk of atrial fibrillation in patients with newly diagnosed type 2 diabetes mellitus: a nationwide population-based study, Diabetes Care 44 (6) (2021) 1393–1401, https://doi.org/10.2337/DC20-2607.
[45] S.C. Larsson, N. Drca, M. Jensen-Urstad, A. Wolk, Combined impact of healthy lifestyle factors on risk of atrial fibrillation: prospective study in men and women, Int. J. Cardiol. 203 (2016) 46–49, https://doi.org/10.1016/j.ijcard.2015.10.106.
[46] J. Farré, H.J. Wellens, Philippe Coumel: a founding father of modern arrhythmology, Europace 6 (5) (2004) 464–465, https://doi.org/10.1016/j.eupc.2004.06.001.
[47] A.M. Pritchett, S.J. Jacobsen, D.W. Mahoney, R.J. Rodeheffer, K.R. Bailey, M. M. Redfield, Left atrial volume as an index ofleft atrial size: a population-based study, J. Am. Coll. Cardiol. 41 (6) (2003) 1036–1043, https://doi.org/10.1016/S0735-1097(02)02981-9.
[48] H.S. Abed, C.S. Samuel, D.H. Lau, et al., Obesity results in progressive atrial structural and electrical remodeling: implications for atrial fibrillation, Heart Rhythm 10 (1) (2013) 90–100, https://doi.org/10.1016/j.hrthm.2012.08.043.
[49] G. Iacobellis, M.C. Ribaudo, G. Leto, et al., Influence of excess fat on cardiac morphology and function: study in uncomplicated obesity, Obes. Res. 10 (8) (2002) 767–773, https://doi.org/10.1038/oby.2002.104.
[50] T.M. Munger, Y.X. Dong, M. Masaki, et al., Electrophysiological and hemodynamic characteristics associated with obesity in patients with atrial fibrillation, J. Am. Coll. Cardiol. 60 (9) (2012) 851–860, https://doi.org/10.1016/j.jacc.2012.03.042.
[51] J.S. Healey, S.J. Connolly, Atrial fibrillation: hypertension as a causative agent, risk factor for complications, and potential therapeutic target, Am. J. Cardiol. 91 (10 SUPPL. 1) (2003) 9–14, https://doi.org/10.1016/S0002-9149(03)00227-3.
[52] R.B. Devereux, M.J. Roman, M. Paranicas, et al., Impact of Diabetes on Cardiac Structure and Function the Strong Heart Study, vol. 101, 2000. http://www.circulationaha.org.
[53] T.J. Wang, H. Parise, D. Levy, et al., Obesity and the risk of new-onset atrial fibrillation, JAMA 292 (20) (2004) 2471–2477, https://doi.org/10.1001/jama.292.20.2471.
[54] M.S. Lauer, K.M. Anderson, W.B. Kannel, D. Levy, The impact of obesity on left ventricular mass and geometry. The Framingham Heart Study, JAMA 266 (2) (1991) 231–236. http://www.ncbi.nlm.nih.gov/pubmed/1829117.
[55] C.J. Lavie, A. Pandey, D.H. Lau, M.A. Alpert, P. Sanders, Obesity and atrial fibrillation prevalence, pathogenesis, and prognosis, J. Am. Coll. Cardiol. 70 (16) (2017) 2022–2035, https://doi.org/10.1016/j.jacc.2017.09.002.
[56] S. Engeli, A.M. Sharma, The renin-angiotensin system and natriuretic peptides in obesity-associated hypertension, J Mol Med 79 (1) (2001) 21–29, https://doi.org/10.1007/s001090000144.
[57] M. Pelat, P. Verwaerde, C. Merial, et al., Impaired atrial M 2-cholinoceptor function in obesity-related hypertension. http://www.hypertensionaha.org, 1999.
[58] N. Calvo, P. Ramos, S. Montserrat, et al., Emerging risk factors and the dose–response relationship between physical activity and lone atrial fibrillation: a prospective case–control study, Europace 18 (1) (2016) 57–63, https://doi.org/10.1093/europace/euv216.
[59] K.A. Heitmann, B. Welde, M.L. Løchen, M. Stylidis, H. Schirmer, B. Morseth, Longitudinal associations between cumulative physical activity and change in structure and function of the left side of the heart: the tromsø study 2007–2016, Front Cardiovasc Med 9 (2022), https://doi.org/10.3389/fcvm.2022.882077.

[60] D. Linz, U. Schotten, H.R. Neuberger, M. Böhm, K. Wirth, Negative tracheal pressure during obstructive respiratory events promotes atrial fibrillation by vagal activation, Heart Rhythm 8 (9) (2011) 1436–1443, https://doi.org/10.1016/j.hrthm.2011.03.053.

[61] Y.K. Iwasaki, Y. Shi, B. Benito, et al., Determinants of atrial fibrillation in an animal model of obesity and acute obstructive sleep apnea, Heart Rhythm 9 (9) (2012) 1409–1416.e1, https://doi.org/10.1016/j.hrthm.2012.03.024.

[62] D. Linz, F. Mahfoud, U. Schotten, et al., Renal sympathetic denervation suppresses postapneic blood pressure rises and atrial fibrillation in a model for sleep apnea, Hypertension 60 (1) (2012) 172–178, https://doi.org/10.1161/HYPERTENSIONAHA.112.191965.

[63] D. Linz, M. Hohl, A. Nickel, et al., Effect of renal denervation on neurohumoral activation triggering atrial fibrillation in obstructive sleep apnea, Hypertension 62 (4) (2013) 767–774, https://doi.org/10.1161/HYPERTENSIONAHA.113.01728.

[64] D. Linz, B. Linz, M. Hohl, M. Böhm, Atrial arrhythmogenesis in obstructive sleep apnea: therapeutic implications, Sleep Med. Rev. 26 (2016) 87–94, https://doi.org/10.1016/j.smrv.2015.03.003.

[65] M. Gao, L. Zhang, B.J. Scherlag, et al., Low-level vagosympathetic trunk stimulation inhibits atrial fibrillation in a rabbit model of obstructive sleep apnea, Heart Rhythm 12 (4) (2015) 818–824, https://doi.org/10.1016/j.hrthm.2014.12.024.

[66] M. Ghias, B.J. Scherlag, Z. Lu, et al., The role of ganglionated plexi in apnea-related atrial fibrillation, J. Am. Coll. Cardiol. 54 (22) (2009) 2075–2083, https://doi.org/10.1016/j.jacc.2009.09.014.

[67] H. Dimitri, M. Ng, A.G. Brooks, et al., Atrial remodeling in obstructive sleep apnea: implications for atrial fibrillation, Heart Rhythm 9 (3) (2012) 321–327, https://doi.org/10.1016/j.hrthm.2011.10.017.

[68] D.D. Mcmanus, X. Yin, R. Gladstone, et al., Alcohol consumption, left atrial diameter, and atrial fibrillation, J. Am. Heart Assoc. 5 (9) (2016), https://doi.org/10.1161/JAHA.116.004060.

[69] G. Thanassoulis, J.M. Massaro, C.J. O'Donnell, et al., Pericardial fat is associated with prevalent atrial fibrillation: the framingham heart study, Circ Arrhythm Electrophysiol 3 (4) (2010) 345–350, https://doi.org/10.1161/CIRCEP.109.912055.

[70] Y.K. Lin, Y.J. Chen, S.A. Chen, Potential atrial arrhythmogenicity of adipocytes: implications for the genesis of atrial fibrillation, Med. Hypotheses 74 (6) (2010) 1026–1029, https://doi.org/10.1016/j.mehy.2010.01.004.

[71] Q. Zhang, T. Liu, C.Y. Ng, G. Li, Diabetes mellitus and atrial remodeling: mechanisms and potential upstream therapies, Cardiovasc Ther 32 (5) (2014) 233–241, https://doi.org/10.1111/1755-5922.12089.

[72] T. Mazurek, L.F. Zhang, A. Zalewski, et al., Human epicardial adipose tissue is a source of inflammatory mediators, Circulation 108 (20) (2003) 2460–2466, https://doi.org/10.1161/01.CIR.0000099542.57313.C5.

[73] S.v. Pandit, J. Anumonwo, J. Jalife, Atrial fibrillation susceptibility in obesity, Circ. Res. 118 (10) (2016) 1468–1471, https://doi.org/10.1161/CIRCRESAHA.116.308686.

[74] R.J. Aviles, D.O. Martin, C. Apperson-Hansen, et al., Inflammation as a risk factor for atrial fibrillation, Circulation 108 (24) (2003) 3006–3010, https://doi.org/10.1161/01.CIR.0000103131.70301.4F.

[75] Y.T. Zhou, P. Grayburn, A. Karim, et al., Lipotoxic heart disease in obese rats: implications for human obesity, Proc. Natl. Acad. Sci. USA 97 (4) (2000) 1784–1789, https://doi.org/10.1073/pnas.97.4.1784.

[76] M. Al-Rawahi, R. Proietti, G. Thanassoulis, Pericardial fat and atrial fibrillation: epidemiology, mechanisms and interventions, Int. J. Cardiol. 195 (2015) 98–103, https://doi.org/10.1016/j.ijcard.2015.05.129.

[77] A. Goette, U. Lendeckel, Electrophysiological effects of angiotensin II. Part I: signal transduction and basic electrophysiological mechanisms, Europace 10 (2) (2008) 238–241, https://doi.org/10.1093/europace/eum283.

[78] A. Zagrosek, D. Messroghli, O. Schulz, R. Dietz, J. Schulz-Menger, Effect of binge drinking on the heart as assessed by cardiac magnetic resonance imaging, JAMA 304 (12) (2010) 1328, https://doi.org/10.1001/jama.2010.1343.

[79] H. Shan, Y. Zhang, Y. Lu, et al., Downregulation of miR-133 and miR-590 contributes to nicotine-induced atrial remodelling in canines, Cardiovasc. Res. 83 (3) (2009) 465–472, https://doi.org/10.1093/cvr/cvp130.

[80] M. Watanabe, H. Yokoshiki, H. Mitsuyama, K. Mizukami, T. Ono, H. Tsutsui, Conduction and refractory disorders in the diabetic atrium, Am. J. Physiol. Heart Circ. Physiol. 303 (2012) 86–95, https://doi.org/10.1152/ajpheart.00010.2012.-Diabetes.

[81] J.W. Waks, M.E. Josephson, Mechanisms of atrial fibrillation – reentry, rotors and reality, Arrhythm Electrophysiol Rev 3 (2) (2014) 90, https://doi.org/10.15420/aer.2014.3.2.90.

[82] D.H. Lau, H.A. Shenasa, M. Shenasa, Hypertension, prehypertension, hypertensive heart disease, and atrial fibrillation, Card Electrophysiol Clin 13 (1) (2021) 37–45, https://doi.org/10.1016/j.ccep.2020.11.009.

[83] M. Mitašíková, H. Lin, T. Soukup, I. Imanaga, N. Tribulová, Diabetes and thyroid hormones affect connexin-43 and PKC-ε expression in rat heart atria, Physiol. Res. 58 (2009) 211–217. www.biomed.cas.cz/physiolres.

[84] A. Voskoboinik, S. Prabhu, Ling L. han, J.M. Kalman, P.M. Kistler, Alcohol and atrial fibrillation, J. Am. Coll. Cardiol. 68 (23) (2016) 2567–2576, https://doi.org/10.1016/j.jacc.2016.08.074.

[85] A. Voskoboinik, G. Wong, G. Lee, et al., Moderate alcohol consumption is associated with atrial electrical and structural changes: insights from high-density left atrial electroanatomic mapping, Heart Rhythm 16 (2) (2019) 251–259, https://doi.org/10.1016/j.hrthm.2018.10.041.

[86] F. Ravelli, M. Masè, M. Del Greco, M. Marini, M. Disertori, Acute atrial dilatation slows conduction and increases AF vulnerability in the human atrium, J. Cardiovasc. Electrophysiol. 22 (4) (2011) 394–401, https://doi.org/10.1111/j.1540-8167.2010.01939.x.

[87] L.A. Gottlieb, R. Coronel, L.R.C. Dekker, Reduction in atrial and pulmonary vein stretch as a therapeutic target for prevention of atrial fibrillation, Heart Rhythm 20 (2) (2023) 291–298, https://doi.org/10.1016/j.hrthm.2022.10.009.

[88] T.E. Walters, G. Lee, S. Spence, et al., Acute atrial stretch results in conduction slowing and complex signals at the pulmonary vein to left atrial junction, Circ Arrhythm Electrophysiol 7 (6) (2014) 1189–1197, https://doi.org/10.1161/CIRCEP.114.001894.

[89] J. Chen, S.L. Wasmund, M.H. Hamdan, Back to the future: the role of the autonomic nervous system in atrial fibrillation, PACE - Pacing and Clinical Electrophysiology. 29 (4) (2006) 413–421, https://doi.org/10.1111/j.1540-8159.2006.00362.x.

[90] P.S. Chen, L.S. Chen, M.C. Fishbein, S.F. Lin, S. Nattel, Role of the autonomic nervous system in atrial fibrillation, Circ. Res. 114 (9) (2014) 1500–1515, https://doi.org/10.1161/CIRCRESAHA.114.303772.

[91] A. Casanova-Lizón, A. Manresa-Rocamora, A.A. Flatt, J.M. Sarabia, M. Moya-Ramón, Does exercise training improve cardiac-parasympathetic nervous system activity in sedentary people? A systematic review with meta-analysis, Int J Environ Res Public Health 19 (21) (2022), https://doi.org/10.3390/ijerph192113899.

[92] M. Pelat, P. Verwaerde, C. Merial, et al., Impaired atrial M $_2$ -cholinoceptor function in obesity-related hypertension, Hypertension 34 (5) (1999) 1066–1072, https://doi.org/10.1161/01.HYP.34.5.1066.

[93] D.S. Thelle, R. Selmer, K. Gjesdal, et al., Resting heart rate and physical activity as risk factors for lone atrial fibrillation: a prospective study of 309 540 men and women, Heart 99 (23) (2013) 1755–1760, https://doi.org/10.1136/heartjnl-2013-303825.

[94] D.S. Quintana, A.J. Guastella, I.S. Mcgregor, I.B. Hickie, A.H. Kemp, Moderate alcohol intake is related to increased heart rate variability in young adults: implications for health and well-being, Psychophysiology 50 (12) (2013) 1202–1208, https://doi.org/10.1111/psyp.12134.

[95] G.M. Marcus, J.W. Dukes, E. Vittinghoff, et al., A randomized, double-blind, placebo-controlled trial of intravenous alcohol to assess changes in atrial electrophysiology, JACC Clin Electrophysiol 7 (5) (2021) 662–670, https://doi.org/10.1016/j.jacep.2020.11.026.

[96] M.C. Mandyam, V. Vedantham, M.M. Scheinman, et al., Alcohol and vagal tone as triggers for paroxysmal atrial fibrillation, Am. J. Cardiol. 110 (3) (2012) 364–368, https://doi.org/10.1016/j.amjcard.2012.03.033.

[97] T. Mäki, L. Toivonen, P. Koskinen, H. Näveri, M. Härkönen, H. Leinonen, Effect of ethanol drinking, hangover, and exercise on adrenergic activity and heart rate variability in patients with a history of alcohol-induced atrial fibrillation, Am. J. Cardiol. 82 (3) (1998) 317–322, https://doi.org/10.1016/S0002-9149(98)00299-9.

[98] R.S.T. Leung, Sleep-disordered breathing: autonomic mechanisms and arrhythmias, Prog. Cardiovasc. Dis. 51 (4) (2009) 324–338, https://doi.org/10.1016/j.pcad.2008.06.002.

[99] E.M. Kallergis, E.G. Manios, E.M. Kanoupakis, et al., Acute electrophysiologic effects of inhaled salbutamol in humans, Chest 127 (6) (2005) 2057–2063, https://doi.org/10.1378/chest.127.6.2057.

[100] Y.K. Lin, M.S. Lai, Y.C. Chen, et al., Hypoxia and reoxygenation modulate the arrhythmogenic activity of the pulmonary vein and atrium, Clin Sci 122 (3) (2012) 121–132, https://doi.org/10.1042/CS20110178.

[101] A. Vincenti, R. Brambilla, M.G. Fumagalli, R. Merola, S. Pedretti, Onset mechanism of paroxysmal atrial fibrillation detected by ambulatory Holter monitoring, Europace 8 (3) (2006) 204–210, https://doi.org/10.1093/europace/euj043.

[102] M. Haïssaguerre, P. Jaïs, D.C. Shah, et al., Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins, N. Engl. J. Med. 339 (10) (1998) 659–666, https://doi.org/10.1056/NEJM199809033391003.

[103] Y. Hung, L.W. Lo, Y.J. Lin, et al., Characteristics and long-term catheter ablation outcome in long-standing persistent atrial fibrillation patients with non-pulmonary vein triggers, Int. J. Cardiol. 241 (2017) 205–211, https://doi.org/10.1016/j.ijcard.2017.04.050.

[104] E. Balse, S. El-Haou, G. Dillanian, et al., Cholesterol modulates the recruitment of Kv1.5 channels from Rab11-associated recycling endosome in native atrial myocytes, Proc. Natl. Acad. Sci. USA 106 (34) (2009) 14681–14686, https://doi.org/10.1073/pnas.0902809106.

[105] H. Wang, H. Shi, L. Zhang, et al., Nicotine is a potent blocker of the cardiac A-type K+ channels, Circulation 102 (10) (2000) 1165–1171, https://doi.org/10.1161/01.CIR.102.10.1165.

[106] H. Wang, B. Yang, L. Zhang, D. Xu, Z. Wang, Direct block of inward rectifier potassium channels by nicotine, Toxicol. Appl. Pharmacol. 164 (1) (2000) 97–101, https://doi.org/10.1006/taap.2000.8896.

[107] C. Schlatzer, E.I. Schwarz, N.A. Sievi, et al., Intrathoracic pressure swings induced by simulated obstructive sleep apnoea promote arrhythmias in paroxysmal atrial fibrillation, Europace 18 (1) (2015), https://doi.org/10.1093/europace/euv122.

[108] E.L. O'Keefe, J.E. Sturgess, J.H. O'Keefe, S. Gupta, C.J. Lavie, Prevention and treatment of atrial fibrillation via risk factor modification, Am. J. Cardiol. 160 (2021) 46–52, https://doi.org/10.1016/j.amjcard.2021.08.042.

[109] H.S. Abed, A.J. Nelson, J.D. Richardson, et al., Impact of weight reduction on pericardial adipose tissue and cardiac structure in patients with atrial fibrillation, Am. Heart J. 169 (5) (2015) 655–662.e2, https://doi.org/10.1016/j.ahj.2015.02.008.

[110] M.E. Middeldorp, R.K. Pathak, M. Meredith, et al., PREVEntion and regReSsive Effect of weight-loss and risk factor modification on Atrial Fibrillation: the REVERSE-AF study, EP Europace 20 (12) (2018) 1929–1935, https://doi.org/10.1093/europace/euy117.
[111] R.K. Pathak, A. Elliott, M.E. Middeldorp, et al., Impact of CARDIOrespiratory FITness on arrhythmia recurrence in obese individuals with atrial fibrillation, J. Am. Coll. Cardiol. 66 (9) (2015) 985–996, https://doi.org/10.1016/j.jacc.2015.06.488.
[112] R.K. Pathak, M. Evans, M.E. Middeldorp, et al., Cost-effectiveness and clinical effectiveness of the risk factor management clinic in atrial fibrillation, JACC Clin Electrophysiol 3 (5) (2017) 436–447, https://doi.org/10.1016/j.jacep.2016.12.015.
[113] Z. Zhao, X. Niu, Z. Dong, et al., Upstream therapeutic strategies of valsartan and fluvastatin on hypertensive patients with non-permanent atrial fibrillation, Cardiovasc Ther 36 (6) (2018), https://doi.org/10.1111/1755-5922.12478.
[114] Z. Zhao, Y. Yang, J. Wang, et al., Combined treatment with valsartan and fluvastatin to delay disease progression in nonpermanent atrial fibrillation with hypertension: a clinical trial, Clin. Cardiol. 43 (12) (2020) 1592–1600, https://doi.org/10.1002/clc.23487.
[115] E. Donnellan, O.M. Wazni, M. Kanj, et al., Impact of risk-factor modification on arrhythmia recurrence among morbidly obese patients undergoing atrial fibrillation ablation, J. Cardiovasc. Electrophysiol. 31 (8) (2020) 1979–1986, https://doi.org/10.1111/jce.14607.
[116] G. Peigh, J. Wasserlauf, K. Vogel, et al., Impact of pre-ablation weight loss on the success of catheter ablation for atrial fibrillation, J. Cardiovasc. Electrophysiol. 32 (8) (2021) 2097–2104, https://doi.org/10.1111/jce.15141.
[117] N. Gessler, S. Willems, D. Steven, et al., Supervised Obesity Reduction Trial for AF ablation patients: results from the SORT-AF trial, EP Europace 23 (10) (2021) 1548–1558, https://doi.org/10.1093/europace/euab122.
[118] R.M.J. Van Der Velden, M.J.M. Hereijgers, N. Arman, et al., Implementation of a screening and management pathway for chronic obstructive pulmonary disease in patients with atrial fibrillation, Europace 25 (7) (2023) 1–10, https://doi.org/10.1093/europace/euad193.
[119] N. Lowres, J. Redfern, Freedman S. Ben, et al., Choice of health options in prevention of cardiovascular events for people with atrial fibrillation (CHOICE-AF): a pilot study, Eur. J. Cardiovasc. Nurs. 15 (1) (2016) 39–46, https://doi.org/10.1177/1474515114549687.
[120] J. Bittman, C.J. Thomson, L.A. Lyall, et al., Effect of an exercise and nutrition program on quality of life in patients with atrial fibrillation: the atrial fibrillation lifestyle project (ALP), CJC Open 4 (8) (2022) 685–694, https://doi.org/10.1016/j.cjco.2022.04.004.
[121] A.M. Joensen, P.T. Dinesen, L.T. Svendsen, et al., Effect of patient education and physical training on quality of life and physical exercise capacity in patients with paroxysmal or persistent atrial fibrillation: a randomized study, J. Rehabil. Med. 51 (6) (2019) 442–450, https://doi.org/10.2340/16501977-2551.
[122] Li L, Alonso A, Romaguera D, et al. Effect of an Intensive Lifestyle Intervention on Circulating Biomarkers of Atrial Fibrillation-Related Pathways Among Adults with Metabolic Syndrome. doi:10.1101/2023.04.28.23288131.
[123] S. Mohanty, P. Mohanty, V. Natale, et al., Impact of weight loss on ablation outcome in obese patients with longstanding persistent atrial fibrillation, J. Cardiovasc. Electrophysiol. 29 (2) (2018), https://doi.org/10.1111/jce.13394.
[124] J.M.L. Hendriks, R. de Wit, H.J.G.M. Crijns, et al., Nurse-led care vs. usual care for patients with atrial fibrillation: results of a randomized trial of integrated chronic care vs. routine clinical care in ambulatory patients with atrial fibrillation, Eur. Heart J. 33 (21) (2012) 2692–2699, https://doi.org/10.1093/eurheartj/ehs071.
[125] J.M.L. Hendriks, R.G. Tieleman, H.J.M. Vrijhoef, et al., Integrated specialized atrial fibrillation clinics reduce all-cause mortality: post hoc analysis of a randomized clinical trial, EP Europace 21 (12) (2019) 1785–1792, https://doi.org/10.1093/europace/euz209.
[126] J.M.L. Hendriks, H.J.M. Vrijhoef, H.J.G.M. Crijns, H.P. Brunner-La Rocca, The effect of a nurse-led integrated chronic care approach on quality of life in patients with atrial fibrillation, Europace 16 (4) (2014) 491–499, https://doi.org/10.1093/europace/eut286.
[127] C. Olivia, C. Hastie, A. Farshid, Adherence to guidelines regarding anticoagulation and risk factors for progression of atrial fibrillation in a nurse-led clinic, Intern. Med. J. 51 (7) (2021) 1136–1142, https://doi.org/10.1111/imj.14874.
[128] B.Q. Abadie, B. Hansen, J. Walker, et al., An atrial fibrillation transitions of care clinic improves atrial fibrillation quality metrics, JACC Clin Electrophysiol 6 (1) (2020) 45–52, https://doi.org/10.1016/j.jacep.2019.09.001.
[129] E.P.J.P. Wijtvliet, R.G. Tieleman, I.C. van Gelder, et al., Nurse-led vs. usual-care for atrial fibrillation, Eur. Heart J. 41 (5) (2019) 642–644, https://doi.org/10.1093/eurheartj/ehz666.
[130] C.J. van den Dries, S. van Doorn, F.H. Rutten, et al., Integrated management of atrial fibrillation in primary care: results of the ALL-IN cluster randomized trial, Eur. Heart J. 41 (30) (2020) 2836–2844, https://doi.org/10.1093/eurheartj/ehaa055.
[131] S. Stewart, J. Ball, J.D. Horowitz, et al., Standard versus atrial fibrillation-specific management strategy (SAFETY) to reduce recurrent admission and prolong survival: pragmatic, multicentre, randomised controlled trial, Lancet 385 (9970) (2015) 775–784, https://doi.org/10.1016/S0140-6736(14)61992-9.
[132] L. Carter, M. Gardner, K. Magee, et al., An integrated management approach to atrial fibrillation, J. Am. Heart Assoc. 5 (1) (2016), https://doi.org/10.1161/JAHA.115.002950.
[133] J.L. Bowyer, P.J. Tully, A.N. Ganesan, F.K. Chahadi, C.B. Singleton, A. D. McGavigan, A randomised controlled trial on the effect of nurse-led educational intervention at the time of catheter ablation for atrial fibrillation on quality of life, symptom severity and rehospitalisation, Heart Lung Circ. 26 (1) (2017) 73–81, https://doi.org/10.1016/j.hlc.2016.04.024.
[134] Y. Vanharen, J.P. Abugattas de Torres, B. Adriaenssens, et al., Nurse-led care after ablation of atrial fibrillation: a randomized controlled trial, Eur J Prev Cardiol (April 17, 2023), https://doi.org/10.1093/eurjpc/zwad117. Published online.
[135] G. Hindricks, T. Potpara, N. Dagres, et al., 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS), Eur. Heart J. 42 (5) (2021) 373–498, https://doi.org/10.1093/eurheartj/ehaa612.
[136] M.K. Chung, L.L. Eckhardt, L.Y. Chen, et al., Lifestyle and risk factor modification for reduction of atrial fibrillation: a scientific statement from the American heart association, Circulation (2020) E750–E772, https://doi.org/10.1161/CIR.0000000000000748. Published online.
[137] H.L. Hsieh, C.W. Kao, S.M. Cheng, Y.C. Chang, A web-based integrated management program for improving medication adherence and quality of life, and reducing readmission in patients with atrial fibrillation: randomized controlled trial, J. Med. Internet Res. 23 (9) (2021), https://doi.org/10.2196/30107.
[138] L. Knaepen, M. Delesie, J. Vijgen, et al., Adherence to oral anticoagulation measured by electronic monitoring in a Belgian atrial fibrillation population, Clin. Res. Cardiol. (2023), https://doi.org/10.1007/s00392-023-02261-w. Published online.
[139] Y. Guo, D.A. Lane, L. Wang, et al., Mobile health technology to improve care for patients with atrial fibrillation, J. Am. Coll. Cardiol. 75 (13) (2020) 1523–1534, https://doi.org/10.1016/j.jacc.2020.01.052.
[140] Y. Yao, Y. Guo, G.Y.H. Lip, The effects of implementing a mobile health-technology supported pathway on atrial fibrillation-related adverse events among patients with multimorbidity: the mAFA-II randomized clinical trial, JAMA Netw. Open (2021), https://doi.org/10.1001/jamanetworkopen.2021.40071. Published online.
[141] K. Hickey, E. Wan, H. Garan, et al., A nurse-led approach to improving cardiac lifestyle modification in an atrial fibrillation population, Journal of Innovations in Cardiac Rhythm Management 10 (9) (2019) 3826–3835, https://doi.org/10.19102/icrm.2019.100902.
[142] L.R. Mitrani, I. Goldenthal, J. Leskowitz, et al., Risk factor management of atrial fibrillation using mHealth: the atrial fibrillation – helping address care with remote technology (AF-HEART) pilot study, Cardiovasc Digit Health J 3 (1) (2022) 14–20, https://doi.org/10.1016/j.cvdhj.2021.11.003.
[143] S. Mohanty, C. Trivedi, D.G. Della Rocca, et al., Impact of digital monitoring on compliance and outcome of lifestyle-change measures in patients with coexistent atrial fibrillation and obesity, Cardiovasc Digit Health J 3 (2) (2022) 75–79, https://doi.org/10.1016/j.cvdhj.2022.01.001.
[144] G.M. Marcus, M.F. Modrow, C.H. Schmid, et al., Individualized studies of triggers of paroxysmal atrial fibrillation: the I-STOP-AFib randomized clinical trial, JAMA Cardiol 7 (2) (2022) 167–174, https://doi.org/10.1001/jamacardio.2021.5010.
[145] M.T. Barrio-Lopez, M. Ruiz-Canela, P. Ramos, et al., PREvention of recurrent arrhythmias with Mediterranean diet (PREDIMAR) study in patients with atrial fibrillation: rationale, design and methods, Am. Heart J. 220 (2020) 127–136, https://doi.org/10.1016/j.ahj.2019.10.009.
[146] K. Štolbová, P. Novodvorský, I. Jakubíková, et al., Effect of complex weight-reducing interventions on rhythm control in obese individuals with atrial fibrillation following catheter ablation: a study protocol, Adv. Ther. 38 (4) (2021), https://doi.org/10.1007/s12325-021-01667-0.
[147] J. Vermeer, T. Vinck, B. de Louw, et al., Improving outcomes of AF ablation by integrated personalized lifestyle interventions: rationale and design of the prevention to improve outcomes of PVI (POP) trial, Clin. Res. Cardiol. 112 (6) (2023) 716–723, https://doi.org/10.1007/s00392-023-02185-5.