Revisiting the risks of incident atrial fibrillation: a narrative review. Part 2

Gaurav Panchal[1], Maria Mahmood[1], Gregory Y.H. Lip[1,2,3]

1 Institute of Applied Health Research, University of Birmingham, Birmingham, United Kingdom
2 Liverpool Centre for Cardiovascular Science, University of Liverpool and Liverpool Heart & Chest Hospital, Liverpool, United Kingdom
3 Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

KEY WORDS
atrial fibrillation, prevention, risk factors

ABSTRACT
Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia with increasing incidence worldwide. Much focus has been directed towards AF prevention, given the morbidity and mortality from stroke, heart failure, and dementia. There are a number of common conditions associated with the onset of AF including, but not limited to, increased alcohol consumption, body weight, exercise, and stress. To reduce the incidence of AF, public health campaigns and targeted patient interventions may be warranted to promote balanced alcohol intake, appropriate exercise, and stress management to prevent AF and associated comorbidity. In this narrative review, we consider the evidence linking these risk factors with AF, putative mechanisms underlying the association, and whether risk factor modification may reduce AF burden.

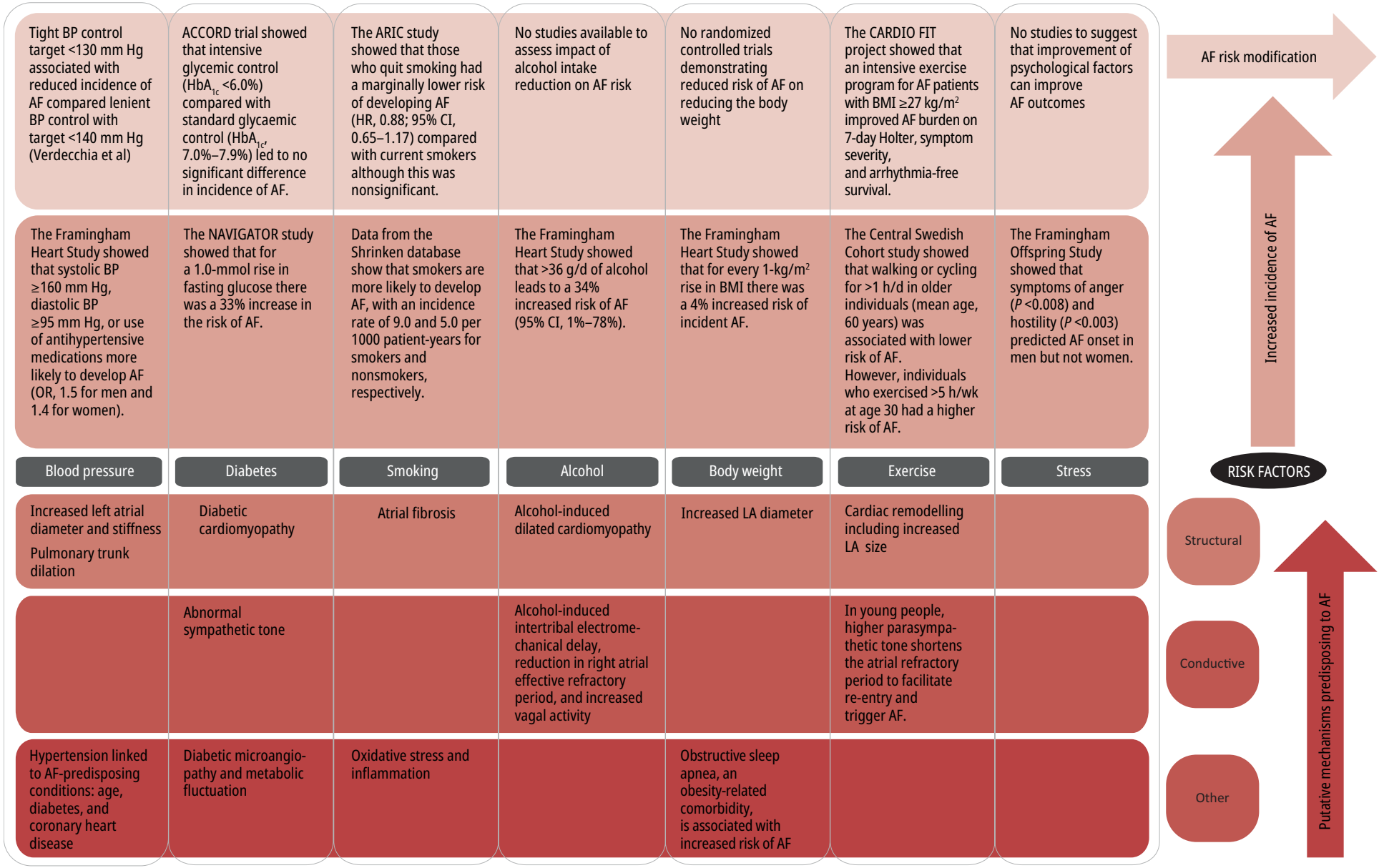
Correspondence to:
Gregory Y.H. Lip, Liverpool, Centre for Cardiovascular Science, University of Liverpool and Liverpool Heart & Chest Hospital, Liverpool, United Kingdom, email: gregory.lip@liverpool.ac.uk
Received: March 30, 2019.
Accepted: April 1, 2019.
Published online: May 24, 2019.
Kardiol Pol. 2019; 77 (5): 515-524
doi:10.33963/KP.14846

Introduction There is increasing recognition that atrial fibrillation (AF) is associated with a higher risk of stroke, heart failure, dementia, and reduced quality of life.[1-5] As the risk of AF is almost 25% after the age of 40 years[6,7] and it is estimated that 4% of the United Kingdom population will have AF by 2050,[8] it follows that AF prevention is a key public health concern.

There are a number of common conditions connected with the onset of AF, including hypertension, diabetes mellitus, smoking, alcohol consumption, increased body weight, exercise, and stress. This narrative review is divided into 2 parts. In Part 1, we discussed the relationship between AF and hypertension, diabetes, and smoking. In Part 2, we examine the evidence supporting the association between AF and alcohol consumption, increased body weight, exercise, and psychosocial factors. FIGURE 1 summarizes the risk factors for AF as discussed in Part 1 and Part 2.

Alcohol The relationship between alcohol and AF has been demonstrated by a number of large-scale studies (TABLE 1), although there is some disagreement regarding the quantity of alcohol conferring the increased risk. For instance, the Copenhagen City Heart Study suggested that a threshold of 35 or more drinks per week (beer, wine, or liquor) was associated with an increased risk of AF (hazard ratio [HR], 1.45; 95% CI, 1.02–2.04), and this increased risk was retained even after adjusting for blood pressure and coronary artery disease (HR, 1.63; 95% CI 1.15–2.31).[9] Alternatively, the Framingham Heart Study matched each new case of AF to 5 controls based on age, sex, hypertension, congestive heart failure, and myocardial infarction to demonstrate that "moderate" long-term alcohol use (defined as <36 g/d) was not associated with significantly increased risk of AF, whereas more than 36 g of alcohol per day led to a 34% increased risk of AF (95% CI, 1%–78%).[10]

The linear dose-relationship between alcohol intake and AF has been demonstrated by a meta-analysis of 12 554 individuals showing that 1 drink per day increased risk of AF by 8% (6%–10%). This study additionally considered the impact of different alcoholic beverages, such that liquor (P for trend = 0.0002) and wine (P for trend = 0.01) were associated with higher risk of AF, but beer was



Abbreviations: AF, atrial fibrillation; ARIC, Atherosclerosis Risk in Communities; BMI, body mass index; BP, blood pressure; HbA_{1c}, glycated hemoglobin A_{1c}; HR, hazard ratio; LA, left atrial; OR, odds ratio

FIGURE 1 Risk factors for atrial fibrillation: mechanisms, increased incidence of atrial fibrillation, and modification

TABLE 1 Amount of alcohol intake and the association with incident atrial fibrillation

Study	Study duration	Population, n	AF events, n	Population characteristics	Reference compared	Adjusted HR (95% CI)		
Cohort of Swedish Men and Swedish Mammography Cohort[11]	Late 1997; follow-up, 12 y	68 848	6019	Age, 45–83 y; men, 55%	<1 drink/wk	1.13 (1.05–1.22) for binge drinking 1.01 (0.94–1.09) for 1–6 drinks/wk 1.07 (0.98–1.17) for 7–14 drinks/wk 1.14 (1.01–1.28) for 15–21 drinks/wk 1.39 (1.22–1.58) for >21 drinks/wk		
Framingham Study[10]	>50	4672	1055	Age, 28–62 y; Framingham Heart Study	None	1.00 (reference)		
					0.1–12.0 g/d	0.97 (0.78–1.22)		
					12.1–24.0 g/d	1.06 (0.80–1.38)		
					24.1–36.0 g/d	1.12 (0.80–1.55)		
					>36.0 g/d	1.34 (1.01–1.78)		
Copenhagen City Heart Study[9]	1976	16 415	1071	Age, 25–75 y; men, 46%; Copenhagen-based cohort; no cardiovascular risk factor or AF		Men	1–6 drinks/wk	
							7–13 drinks/wk	
							14–20 drinks/wk	
							≥21 drinks/wk	
						Women	1–6 drinks/wk	
							7–13 drinks/wk	
							≥14 drinks per week	
Women's Health Study[14]	1993–2006, follow-up, 12.4 y	34 715	653	Age, ≥45 y; mean age, 53 y; white patients, 94.3%	Nondrinkers	0–1 drinks/d	1.11 (0.75–1.65)	
						1–2 drinks/d	≥14 drinks per week	
						≥2 drinks/d	1.19 (0.55–2.57)	
Danish Diet, Cancer, and Health Study[13]	1993–1997; follow-up, 5.7 y	47 949	556	Mean age, 54 y; men, 47%	Lowest quantile	Quantile 2	Men	1.04 (0.73–1.49)
							Women	1.09 (0.68–1.75)
						Quantile 3	Men	1.44 (1.04–2.01)
							Women	1.27 (0.80–2.04)
						Quantile 4	Men	1.25 (0.89–1.76)
							Women	1.23 (0.77–1.98)
						Quantile 5	Men	1.46 (1.05–2.04)
							Women	1.14 (0.70–1.85)
ONTARGET and TRANSCEND[12]	2001–2004	30433	2093	Age, ≥55 y; mean age, 66.4 y; men, 70.2%; history of cardiovascular disease or diabetes with end-organ damage	<1 drink/wk	1.14 (1.04–1.26) for 1–21 drinks/wk for men and 1–14 drinks/wk for women 1.32 (0.97–1.80) for >3 drinks/d for men and >2 drinks/d for women		

Abbreviations: ONTARGET, Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial; TRANSCEND, Telmisartan Randomized Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease; others, see FIGURE 1

nonsignificant (P = 0.28). Importantly, both moderate (1–3 drinks per day) and high (>3 drinks per day) alcohol intake was associated with increased risk of AF.[11] Furthermore, data from the TRANSCEND (Telmisartan Randomized Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease) and the ONTARGET (Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial) cohorts showed that both moderate (defined as 1–14 drinks per week) and high (>14 drinks per week) alcohol intake was associated with increased risk of AF (HR, 1.14; 95% CI, 1.04–1.26 and HR, 1.32; 95% CI, 0.97–1.80; respectively; P = 0.002). Notably, among moderate drinkers, those who engaged in binge drinking (>5 drinks per day) had a higher risk of AF (HR, 1.29; 95% CI, 1.02–1.62).[12]

The relationship between alcohol and AF has been examined in both men and women, with contradicting results. The Danish Diet, Cancer and Health Study suggested that there was a dose-response correlation between alcohol consumption and AF in men (P = 0.04); however, women drinking moderate amounts of alcohol did not have an increased risk of AF (P = 0.69). The authors suggested that fewer AF outcomes in women may have confounded their results.[13] On the other hand, the Women's Health Study showed that drinking up to 2 alcoholic beverages per week did not increase the risk of AF, but intake of more than 2 alcoholic drinks per week was associated with higher incidence of AF (2.25 events per 1000 person-years) compared with nondrinkers (0.66 events per 1000 person-years).[14]

The potential mechanisms that underlie the association between alcohol and AF may be divided into conductive or structural. Conductive causes include alcohol-induced intertribal electromechanical delay,[15] reduction of the right atrial effective refractory period,[16] as well as increased vagal activity.[17] Structural changes include oxidative stress[18,19] and morphological changes such as dilated cardiomyopathy.[20-22]

In summary, alcohol consistently increases the risk of AF (8% per drink per day) in proportion to the amount of alcohol consumed. Avoiding binge drinking and minimizing intake of alcohol should be encouraged at every point of medical contact. However, studies to assess long-term impact of reducing alcohol intake on AF risk are needed.

Body weight and atrial fibrillation The association between body weight and AF onset has been explored in a number of studies utilizing data (TABLE 2) accumulated for patients initially recruited as early as the 1970s.

The Multifactor Primary Prevention Study was a prospective study of 7495 men between the age of 47 and 55 years, conducted in Goteborg, Sweden, which showed that high body mass index (BMI) was an independent risk factor for the development of AF (HR, 1.07; 95% CI, 1.04–1.10).[23,24] The Framingham Heart Study further suggested that for every unit rise in BMI, there was a 4% increased risk of incident AF. Notably, obese individuals were more likely to have enlarged left atrial (LA) diameter (P <0.001), and LA diameter was strongly associated with AF onset (P <0.001). When adjusted for LA diameter, the relationship between AF and high BMI was no longer significant (P = 0.84 and P = 0.56 for men and women, respectively).[25]

The Renfrew-Paisley study also suggested that elevated BMI (≥30 kg/m^2) was associated with increased risk of AF (HR, 1.75; 95% CI, 1.17–2.65).[25] However, the key limitation was that the influence of obesity-related conditions such as diabetes, hypertension, and hypercholesterolemia were not accounted for in the multivariable analysis.[26] It was the Danish Diet, Cancer and Health Study which demonstrated that the increase in AF risk per unit rise in BMI (HR, 1.08; 95% CI, 1.05–1.11 for men and HR, 1.06; 95% CI, 1.03–1.09 for women) persisted in the absence of obesity-related comorbidity.[27]

One obesity-related comorbidity that has been proposed to increase the risk of incident AF is obstructive sleep apnea. Gami et al[28] retrospectively studied 3542 patients who attended the Mayo Sleep Clinic for diagnostic polysomnography between 1987 and 2003. The authors observed that both obesity (per 1 kg/m^2; HR, 1.07; 95% CI, 1.05–1.10) and the magnitude of nocturnal oxygen desaturation (per 0.5 U log change; HR, 3.29; 95% CI, 1.35–8.04) secondary to obstructive sleep apnea increased the risk of AF.

In addition, data from the Women's Health Study have been used to consider the influence of weight at different times in life on AF risk.[29,30] First, it was demonstrated that higher birth weight led to an incremental risk of developing AF (P for linear trend = 0.002).[29] The fact that adjustment for adult height and maximum weight attenuated the linear trend (P = 0.004 and P = 0.23, respectively) suggests that although birthweight may influence the risk of AF, this may be in part due to high birth weight predicting elevated BMI in adult life.[29] Furthermore, AF risk was found to be increased with both short-term (18%) and long-term (41% over 60 months) rise in BMI.[30] Another study in a male cohort revealed that development of AF was associated with both body surface area at the age of 20 years (P <0.0001) and weight gain from the age of 20 years to midlife (P <0.0001), suggesting that lifestyle choices in youth may influence the risk of AF in older age.

In summary, increased body weight predicts future risk of AF, and it is one of the strongest predisposing factors for AF. In addition to being an independent risk factor, obesity is also associated with various other cardiovascular diseases that can increase the risk of AF.

Exercise and cardiorespiratory effort The relationship between AF incidence and physical exercise is complex, and the available data (TABLE 3) suggest that it depends both on the age of the individual and the quantity of exercise.

The Central Swedish Cohort study showed that individuals who exercised more than 5 hours per week at the age of 30 years had a higher risk of developing AF (relative risk, 1.19; 95% CI, 1.05–1.36; P = 0.008) compared with men who had exercised less than 1 hour per week at the same age.[31] Alternatively, walking or cycling for more than 1 hour per day in older individuals (mean age, 60 years) was associated with lower risk of AF (RR, 0.87; 95% CI, 0.77–0.97).[31] Taken

TABLE 2 Body weight and atrial fibrillation

Study	Study duration	Follow-up, y	Study population, n	Population characteristics	AF events, n	Study group	Adjusted HR (95% CI)	Conclusion
Multifactor Primary prevention study[23,24]	1970–1973	Mean, 25.2	7437	AF on ECG; men aged 47–55 y	754	BMI ≥27 kg/m^2	1.35 (1.17–1.57)	Weight gain is associated with increased AF risk.
	1970–2004	Max, 3.3	6903	Mean age, 51.5 y; single midlife evaluation	1253	4%–15% weight gain from age 20	1.16 (0.96–1.41)	Weight gain from age 20 to midlife is independently related to the development of AF.
						16%–35% weight gain from age 20	1.46 (1.17–1.81)	
						>35% weight gain from age 20	1.90 (1.37–2.64)	
Women's Health Study[29]	1993–2004	14.5	34309	Women, 100%; mean age, 54 y; white, 95%	834	BMI, 25–29.9 kg/m^2,	1.22 (1.02–1.45)	High BMI was associated with a short- and long-term increase in AF risk.
						BMI ≥30 kg/m^2	1.65 (1.36–2.00)	
Women's Health Study[30]			27982	Women >45 y and free of cardiovascular disease and AF at baseline	735	Birth weight, 2.5–3.2 kg	1.27 (0.94–1.71)	Birth weight was associated with incident AF. Higher birthweight was associated with increased AF incidence.
						Birth weight, 3.2–3.9 kg	1.10 (0.83–1.46)	
						Birth weight, 3.9 −4.5 kg	1.41 (1.01–1.96)	
						Birth weight >4.5 kg	1.29 (0.84–1.98)	
Framingham Health Study and Framingham Offspring Study[25]	1979–1983	13.7	5282	Mean (SD) age, 57 (13) y; women, 55%; without baseline AF	526	Obese men (BMI ≥30 kg/m^2)	1.52 (1.09–2.13)	There is a dose-response relationship with elevated BMI and risk of AF.
						Obese women (BMI ≥30 kg/m^2)	1.46 (1.03–2.07)	
						Per unit increase in BMI in men and women	1.04 (1.01–1.07)	
Danish Diet, Cancer, and Health[27]	1993–2001	Mean, 5.7	47589	Mean age at baseline, 56 y (range, 50–64 y); men, 47%	553	BMI ≥30 kg/m^2 in men	2.35 (1.70–3.25)	Obesity in both men and women is associated with an increased risk of AF.
						BMI ≥30 kg/m^2 in women	1.99 (1.31–3.02)	
Renfrew-Paisley Study[26]	1972 and 1976	20	15144	AF on ECG; age, 45–64 y; men, 45.7%; living in 2 towns in the west of Scotland	172	BMI ≥30 kg/m^2	1.76 (1.04–2.98) in women	Obesity is associated with an increased risk of AF.
Gami et al[28] (Olmsted County)	1987–2003	4.7	3150	Age <65 y; mean age, 49 y men, 66%	133	BMI >30 kg/m^2	1.48 (1.03–2.12)	Obesity and nocturnal oxygen desaturation increase the risk of AF onset.

Abbreviations: ECG, electrocardiography; other, see FIGURE 1

TABLE 3 Physical activity and the relationship to atrial fibrillation (continued on the next page)

Study	Study duration	Study population, n	Population characteristics	Inclusion criteria	Type of exercise	Exercise stratification	Follow-up, y	AF events	RR (95% CI)	Conclusion
Central Swedish cohort[31]	1997–2009	44 010	All male; age, 45–79 y; mean age, 60 y	Without any cancer or AF	Leisure-time exercise	>5 h/wk at age 30	Median, 12	4568	1.19 (1.05–1.36)	The risk of AF with exercise is dependent on age such that there is an increased risk younger age compared with decreased risk in older age.
						>5 h/wk at age 45–79			1.05 (0.92–1.18)	
					Walking and/or cycling	>1 h/d at age 30			1.08 (0.93–1.27)	
						>1 h/d at ages 45–79			0.88 (0.77–0.998)	
Swedish Mammography Cohort[35]	1998–2009	36 513	All female; age, 49–83 y; mean age, 60 y	AF free	Leisure-time exercise	≥4 h/wk	Median, 12	2915	0.75 (0.67–0.84)	Higher levels of leisure time exercise reduce AF risk in women.
					Walking and/or cycling	≥40 min/d			0.71 (0.63–0.80)	
Women's Health Initiative Observational Study[34]	1994–1998	81 317	Women at postmenopausal age; mean age, 63.8 y; white, 83.9%	Complete data available, no previous AF, not underweight	Various activities	0–3 MET h/wk	Median, 11.5	9792	0.98 (0.91–1.06)	Increased levels of physical activity reduces AF risk even in obese individuals.
						3–9 MET h/wk			0.94 (0.88–1.01)	
						>9 MET h/wk			0.90 (0.85–0.96)	
Andersen et al[33]	1989–2005	52 755	Men, 93.1%; mean (SD) age, 38.5 (12.2) y	All Swedish individuals participating in Vasaloppet skiing event	Skiing	Fastest group	Median (IQR), 9.7 (0.01–16.8)	681	1.20 (0.93–1.55)	Faster completion of cross country skiing events was associated with higher risk of cardiac arrhythmia including AF.
						Finished ≥5 races			1.29 (1.04–1.61)	
Physicians' Health Study[32]	1982–2001	16 921	Physicians, all male; mean age, 51 y	Men; age, 40–84 y, in 1982 with no history of myocardial infarction, stroke, transient ischemic attacks, or cancer	Cycling, jogging, racquet sports, swimming	<1 d of vigorous exercise/wk	Median, 12	1661	1.14 (0.86–1.51)	Higher frequency of vigorous exercise is associated with increased risk of AF in men <50 years and joggers.
						1–2 d of vigorous exercise/wk			1.06 (0.91–1.23)	
						3–4 d of vigorous exercise/wk			1.01 (0.89–1.16)	
						5–7 d of vigorous exercise/wk			1.16 (0.99–1.36)	
Henry Ford Exercise Testing Project[36]	1991–2009	64 561	Mean (SD) age, 54.5 (12.7) y; 46% female; 64% white	All individuals underwent exercise treadmill test in tertiary care center between 1991 and 2009	Variable, only MET assessed on exercise test	1 higher MET achieved during treadmill testing	Median (IQR), 5.4 (3–9)	4616	0.93 (0.92–0.94)	Higher levels of cardiorespiratory fitness were associated with lower rates of incident AF.

TABLE 3 Physical activity and atrial fibrillation (continued from the previous page)

Study	Study duration	Study population, n	Population characteristics	Inclusion criteria	Type of exercise	Exercise stratification	Follow-up, y	AF events	RR (95% CI)	Conclusion
Kuopio Ischemic Heart Disease study[37]	1984–1989	1950	Mean (SD) age, 52.6 (5.1) y; all male	Population-based study	Cycle ergometer exercise test	Mean CRF, 20.3 ml/kg/min	Average, 19.5	91/488	reference	AF risk rises at higher levels of cardiorespiratory fitness.
						Mean CRF, 27.7 ml/kg/min		90/487	0.88 (0.65–1.19)	
						Mean CRF, 32.6 ml/kg/min		56/488	0.70 (0.49–0.99)	
						Mean CRF, 40.6 ml/kg/min		68/487	0.98 (0.66–1.43)	
Cardiorespiratory Fitness Project[45]	–	308	BMI ≥27 kg/m^2; mean age, 62 y; men, 49%	Patients with paroxysmal AF	Exercise stress test	1-MET gain from baseline to follow up (multivariate, risk of recurrence of AF)	Mean (SD), 49 (19) months		HR, 0.88 (0.80–0.96)	Increase in cardiorespiratory fitness is associated with reduced AF burden and severity.
						<2 MET CRF gain			HR, 3.9 (2.1–7.3)	
						No weight loss			HR, 1.9; (1.1–3.70)	
						Low baseline CRF			HR, 5.12; (2.67–9.84)	

Abbreviations: CRF, cardiorespiratory fitness; MET, metabolic equivalent task; RR, relative risk; others, see FIGURE 1

TABLE 4 Psychosocial factors and incident atrial fibrillation

Study	Study duration	Follow-up	Study population, n	Population characteristics	Groups studied	AF events, n	RR (95% CI)	Conclusion
Framingham Offspring Study[46]	1984–1987	10 y	3873	Age, 18–77 y; mean (SD) age, 48.5 (10.1) y; men, 48%	Men, trait anger	194	1.1 (1.0–1.4)	Increase in 10-year risk of AF in men with traits of anger and hostility
					Men, symptoms of anger		1.2 (1.0–1.4)	
					Men, hostility		1.3 (1.1–1.5)	
Framingham Offspring Study[47]	1984–1987	10 y	3682	Age, 18–77 y; mean (SD) age, 48.5 (10.1) y; men, 48%	Men with tension	194	1.24 (1.04–1.48)	Higher levels of tension are associated with an increased risk of AF.
National Health Insurance program in Taiwan[49]	1995–2007	7 y	3888	Mean (SD) age, 42.21 (15.02) y in PD; men, 36%; community-based study in Taiwan	Panic disorder	406	1.73 (1.26–2.37)	Panic disorder is associated with increased risk of AF.
Primary Prevention Study[50]	1974–1977	Until death, hospital discharge, or age 75 y	6035	Mean age, 55.3 y; 50% in white collar job; all men without stroke, AF or CAD	Low-strain job vs high-strain job	436	1.23 (0.84–1.82)	Occupational stressors are associated with a higher risk of AF.
Women's Health Study[48]	1993–2010	Median (IQR), 125 (117–130) mo	30746	All female, 6.8% with significant global psychological stress	Depression or antidepressant use or both	771	0.99 (0.78–1.25)	Risk of AF in women is not associated with psychological distress.

Abbreviations: CAD, coronary artery disease; PD, panic disorder; others, see FIGURE 1 and TABLE 3

together, these data suggest that high levels of exercise may be beneficial in preventing AF onset in older patients but detrimental in younger patients. The Physician Health Study (PHS) similarly observed that men older than 50 years of age who exercised 5 to 7 days per week had an increased risk of AF (RR, 1.69; 95% CI, 1.22–2.33; P = 0.014).[32] The nature of exercise was also relevant as men who regularly jogged were at increased risk of developing AF (P <0.01), whereas there was no increased risk for cycling, swimming, or racquet sports.[32]

Furthermore, Andersen et al[33] explored the relationship between long-distance cross-country skiing and the development of arrhythmia. They noted that individuals who finished a race in shorter time had a higher incidence of AF (HR, 1.20; 95% CI, 0.93–1.55), as did participants completing a higher number of races subsequently (≥5 races; HR, 1.29; 95% CI, 1.04–1.61). While this study further suggests that higher levels of exercise may lead to an increased risk of AF, this was limited by lack of adjustment for possible confounding factors such as smoking, alcohol, blood pressure, and diabetes. The baseline weekly levels of exercise were also not considered.

In contrast to the above studies in men, the Women's Health Initiative Observational Study noted a beneficial effect of exercise on reducing the risk of AF in women.[34] This prospective observational study of 93 767 postmenopausal women assessed physical activity by self-reported questionnaires to determine individual metabolic equivalent tasks (METs) completed per week. There was a clear negative linear dose-response relationship between physical activity and the risk of AF, as the maximum protective effect of exercise was noted for individuals performing more than 9 MET hours per week (HR, 0.90; 95% CI, 0.85–0.96). Moreover, even obese participants who were physically active (>9 MET hours per week) had a lower risk of AF than inactive obese patients.[34] The Swedish Mammography cohort of 36 513 older women (median age, 60 years) similarly noted that the risk of AF decreased with increasing levels of exercise (RR, 0.85; 95% CI, 0.75–0.95 for ≥4 hours per week vs <1 hours per week).[35]

While the previous studies considered exercise frequency and quantity, the Henry Ford Exercise Testing (FIT) project was designed to examine the relationship between cardiorespiratory fitness and incident AF. There was a dose-response relationship between exercise and incident AF such that 1 higher metabolic equivalent achieved in a treadmill exercise test conferred a 7% lower risk of AF (HR, 0.93; 95% CI, 0.92–0.94; P <0.001).[36] Conversely, the KIHD (Kuopio Ischemic Heart disease) study noted that although moderate exercise was associated with a 28% reduction in AF events, the relationship was nonlinear, with an increase in AF incidence during high-intensity exercise.[37]

One putative mechanism underlying the relationship between AF and exercise is that cardiac remodeling in athletes[38,39] may serve as a substrate for the development of AF. Indeed, LA enlargement is a strong predictor of AF in competitive sports.[1,40,41] Perhaps those performing moderate exercise are protected from an increased risk of AF, as they are not exposed to the same hemodynamic changes (compared, for example, with an endurance runner) sufficient to cause cardiac remodeling.[42] In young individuals who perform vigorous physical activity, the higher parasympathetic tone may shorten the atrial refractory period to facilitate re-entry and trigger AF.[43] As parasympathetic tone decreases with aging,[44] the benefit of exercise to reduce the risk of AF may be observed.

The utility of exercise in improving the AF burden was explored in the Cardiorespiratory Fitness (CARDIO FIT) project. The improvement of cardiorespiratory fitness in AF patients with a BMI of 27 kg/m^2 or more who undergo an intensive exercise program was assessed over a mean (SD) of 49 (19) months. It was demonstrated that AF burden on 7-day Holter monitoring, symptom severity, and arrhythmia-free survival were all improved in patients whose MET gain was 2 or more compared with those with a MET gain of less than 2 (all P <0.001).[45]

In summary, there is a mixed response observed with different severities of physical activity and the relationship to incident AF. There may also be a bimodal relationship noted with physical activity. Extremes of physical activity seem to be associated with a rise in the risk of AF, likely due to an effect on the LA structure. However, moderate activity in middle and older age is associated with a significant reduction in AF incidence.

Psychosocial factors, including stress When considering the influence of stress on AF incidence, the available data (TABLE 4) suggest that men may be more susceptible than women.

This aspect was examined in the Framingham Offspring Study, which was a prospective cohort study of 3873 individuals between 18 and 77 years of age, who were followed up for 10 years.[46] Psychosocial questionnaires were emailed and collected at clinic visits. The investigators found that symptoms of anger (P <0.008) and hostility (P <0.003) predicted AF onset in men after adjustment for age, diabetes, hypertension as well as history of myocardial infarction, congestive heart failure, and valvular heart disease; however, there was no association between the above factors and AF onset in women.[46]

Another similar study utilized the Framingham tension and anxiety scales to show that higher levels of tension led to higher mortality

in men and women (RR, 1.22; 95% CI, 1.08–1.38 and RR, 1.27; 95% CI, 1.05–1.55, respectively), although only men had an increased risk of AF (RR, 1.24; 95% CI, 1.04–1.48).[47] This trend was further highlighted by the Women's Health Study, which showed that neither global psychological distress (P = 0.61) nor depression (P = 0.93) was associated with AF incidence in women, albeit individuals who reported that they felt "happy for some/a good bit of the time" had a reduced risk of AF (HR, 0.69; 95% CI, 0.49–0.99; P = 0.04).[48]

Furthermore, there are studies that considered the impact of anxiety and profession and AF onset. Cheng et al[49] observed that patients with panic disorder had a significantly higher risk of AF (HR, 1.73; 95% CI, 1.26–2.37) even after adjustment for age, male sex, hypertension, coronary artery disease, congestive heart failure, and valvular heart disease.[49] In addition, a study of 6035 Swedish men showed that high-strain occupations (HR, 1.32; 95% CI, 1.00–1.73) including local transport driver, bus driver, primary education teacher, docker, freight handler, and baker had a higher risk of AF onset.[50] The limitation of this study was that it only took work-related stress into consideration, whereas other factors such as low socioeconomic status, lack of social support, and domestic circumstances were not accounted for.

In summary, men have an increased risk of AF due to psychological distress, depression, and anger. At present, no studies definitely suggest that improvement of any psychological factors can improve outcomes in patients with AF.

Conclusions It is clear that hypertension, diabetes, smoking, high alcohol consumption, increased body weight, high stress levels, and too much or too little exercise increase the risk of developing AF. Considering the impact of AF-related comorbidity, it is vital that steps are taken to modify these risk factors.

The prevention of AF requires political willingness to encourage various interventions such as exercise, alcohol, and smoking cessation program. Medical professionals must adopt an individualized approach to educate patients at every stage of medical contact. Indeed, these lifestyle efforts may be cost-effective, for example, a recent study quantified an increase of 0.1930 quality-adjusted life years and a cost saving of 12 094 USD for patients with symptomatic AF undergoing aggressive risk factor management compared with controls.[51] Furthermore, aggressive risk factor modification has been shown to reduce AF burden and maintain sinus rhythm[52] as well as improve procedural outcomes following catheter ablation.[53]

Finally, risk factor modification must be considered a key pillar of AF management. For instance, the proposed Atrial fibrillation Better Care (ABC) pathway (A – avoid stroke with anticoagulation; B – better symptom management, and C – cardiovascular and comorbidity risk reduction) provides an integrated approach to the holistic management of AF,[54,55] which has been associated with improved clinical outcomes and lower health care costs.[56-58] Such a streamlined holistic approach should be the way forward for optimizing AF management.

ARTICLE INFORMATION

CONFLICT OF INTEREST GYHL is a consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseon, and Daiichi-Sankyo as well as a speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo. No fees are directly received personally. Other authors have no conflict of interest to declare.

HOW TO CITE Panchal G, Mahmood M, Lip GYH. Revisiting the risks of incident atrial fibrillation: a narrative review. Part 2. Kardiol Pol. 2019; 77: 515-524. doi:10.33963/KP.14846

REFERENCES

1 Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. Am J Cardiol. 1998; 82: 2N-9N.

2 Benjamin EJ, Wolf PA, D'Agostino RB, et al. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation. 1998; 98: 946-952.

3 Thrall G, Lane D, Carroll D, Lip GY. Quality of life in patients with atrial fibrillation: a systematic review. Am J Med. 2006; 119: 448.e1-19.

4 Wang TJ, Larson MG, Levy D, et al. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: the Framingham Heart Study. Circulation. 2003; 107: 2920-2925.

5 Stewart S, Hart CL, Hole DJ, McMurray JJV. A population-based study of the long-term risks associated with atrial fibrillation: 20-year follow-up of the Renfrew/Paisley study. Am J Med. 2002; 113: 359-364.

6 Heeringa J, van der Kuip DA, Hofman A, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. Eur Heart J. 2006; 27: 949-953.

7 Lloyd-Jones DM, Wang TJ, Leip EP, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. Circulation. 2004; 110: 1042-1046.

8 Miyasaka Y, Barnes ME, Gersh BJ, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. Circulation. 2006; 114: 119-125.

9 Mukamal KJ, Tolstrup JS, Friberg J, et al. Alcohol consumption and risk of atrial fibrillation in men and women: the Copenhagen City Heart Study. Circulation. 2005; 112: 1736-1742.

10 Djoussé L, Levy D, Benjamin EJ, et al. Long-term alcohol consumption and the risk of atrial fibrillation in the Framingham Study. Am J Cardiol. 2004; 93: 710-713.

11 Larsson SC, Drca N, Wolk A. Alcohol consumption and risk of atrial fibrillation. J Am Coll Cardiol. 2014; 64: 281-289.

12 Liang Y, Mente A, Yusuf S, et al. Alcohol consumption and the risk of incident atrial fibrillation among people with cardiovascular disease. CMAJ. 2012; 184: E857-E866.

13 Frost L, Vestergaard P. Alcohol and risk of atrial fibrillation or flutter: a cohort study. Arch Intern Med. 2004; 164: 1993-1998.

14 Conen D, Tedrow UB, Cook NR, et al. Alcohol consumption and risk of incident atrial fibrillation in women. JAMA. 2008; 300: 2489-2496.

15 Sengul C, Cevik C, Ozveren O, et al. Acute alcohol consumption is associated with increased interatrial electromechanical delay in healthy men. Cardiol J. 2011; 18: 682-686.

16 Marcus GM, Smith LM, Whiteman D, et al. Alcohol intake is significantly associated with atrial flutter in patients under 60 years of age and a shorter right atrial effective refractory period. Pacing Clin Electrophysiol. 2008; 31: 266-272.

17 Mandyam MC, Vedantham V, Scheinman MM, et al. Alcohol and vagal tone as triggers for paroxysmal atrial fibrillation. Am J Cardiol. 2012; 110: 364-368.

18 Youn JY, Zhang J, Zhang Y, et al. Oxidative stress in atrial fibrillation: an emerging role of NADPH oxidase. J Mol Cell Cardiol. 2013; 62: 72-79.

19 Mihm MJ, Yu F, Carnes CA, et al. Impaired myofibrillar energetics and oxidative injury during human atrial fibrillation. Circulation. 2001; 104: 174-180.

20 George A, Figueredo VM. Alcohol and arrhythmias: a comprehensive review. J Cardiovasc Med. 2010; 11: 221-228.

21 Piano MR. Alcoholic cardiomyopathy: incidence, clinical characteristics, and pathophysiology. Chest. 2002; 121: 1638-1650.

22 Ettinger PO, Wu CF, De La Cruz C, et al. Arrhythmias and the "Holiday Heart": alcohol associated cardiac rhythm disorders. Am Heart J. 1978; 95: 555-562.

23 Rosengren A, Hauptman PJ, Lappas G, et al. Big men and atrial fibrillation: effects of body size and weight gain on risk of atrial fibrillation in men. Eur Heart J. 2009; 30: 1113-1120.

24 Wilhelmsen L, Rosengren A, Lappas G. Hospitalizations for atrial fibrillation in the general male population: morbidity and risk factors. J Intern Med. 2001; 250: 382-389.

25 Wang TJ, Parise H, Levy D, D'Agostino RB Sr, Wolf PA, Vasan RS, et al. Obesity and the risk of new-onset atrial fibrillation. JAMA. 2004; 292: 2471-2477.

26 Murphy NF, MacIntyre K, Stewart S, et al. Long-term cardiovascular consequences of obesity: 20-year follow-up of more than 15 000 middle-aged men and women (the Renfrew–Paisley study). Eur Heart J. 2005; 27: 96-106.

27 Frost L, Hune LJ, Vestergaard P. Overweight and obesity as risk factors for atrial fibrillation or flutter: the Danish Diet, Cancer, and Health Study. Am J Med. 2005; 118: 489-495.

28 Gami AS, Hodge DO, Herges RM, et al. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. J Am Coll Cardiol. 2007; 49: 565-571.

29 Conen D, Tedrow UB, Cook NR, et al. Birth weight is a significant risk factor for incident atrial fibrillation. Circulation. 2010; 122: 764-770.

30 Tedrow UB, Conen D, Ridker PM, et al. The long- and short-term impact of elevated body mass index on the risk of new atrial fibrillation. J Am Coll Cardiol. 2010; 55: 2319-2327.

31 Drca N, Wolk A, Jensen-Urstad M, Larsson SC. Atrial fibrillation is associated with different levels of physical activity levels at different ages in men. Heart. 2014; 100: 1037-1042.

32 Aizer A, Gaziano JM, Cook NR, et al. Relation of vigorous exercise to risk of atrial fibrillation. Am J Cardiol. 2009; 103: 1572-1577.

33 Andersen K, Farahmand B, Ahlbom A, et al. Risk of arrhythmias in 52 755 long-distance cross-country skiers: a cohort study. Eur Heart J. 2013; 34: 3624-3631.

34 Azarbal F, Stefanick ML, Salmoirago-Blotcher E, et al. Obesity, physical activity, and their interaction in incident atrial fibrillation in postmenopausal women. J Am Heart Assoc. 2014; 3: e001127.

35 Drca N, Wolk A, Jensen-Urstad M, Larsson SC. Physical activity is associated with a reduced risk of atrial fibrillation in middle-aged and elderly women. Heart. 2015; 101: 1627-1630.

36 Qureshi WT, Alirhayim Z, Blaha MJ, et al. Cardiorespiratory fitness and risk of incident atrial fibrillation: results from the Henry Ford ExercIse Tesing (FIT) project. Circulation. 2015; 131: 1827-1834.

37 Khan H, Kella D, Rauramaa R, et al. Cardiorespiratory fitness and atrial fibrillation: A population-based follow-up study. Heart Rhythm. 2015; 12: 1424-1430.

38 Hood S, Northcote RJ. Cardiac assessment of veteran endurance athletes: a 12 year follow up study. Br J Sports Med. 1999; 33: 239-243.

39 Kasikcioglu E, Oflaz H, Akhan H, et al. Left atrial geometric and functional remodeling in athletes. Int J Sports Med. 2006; 27: 267-271.

40 Pelliccia A, Maron BJ, Di Paolo FM, et al. Prevalence and clinical significance of left atrial remodeling in competitive athletes. J Am Coll Cardiol. 2005; 46: 690-696.

41 Molina L, Mont L, Marrugat J, et al. Long-term endurance sport practice increases the incidence of lone atrial fibrillation in men: a follow-up study. Europace. 2008; 10: 618-623.

42 Bouchard C, Daw EW, Rice T, et al. Familial resemblance for VO2max in the sedentary state: the HERITAGE family study. Med Sci Sports Exerc. 1998; 30: 252-258.

43 Northcote RJ, McKillop G, Todd IC, Canning GP. The effect of habitual sustained endurance exercise on cardiac structure and function. Eur Heart J. 1990; 11: 17-22.

44 Oida E, Kannagi T, Moritani T, Yamori Y. Aging alteration of cardiac vagosympathetic balance assessed through the tone-entropy analysis. J Gerontol A Biol Sci Med Sci. 1999; 54: M219-M224.

45 Pathak RK, Elliott A, Middeldorp ME, et al. Impact of CARDIOrespiratory FITness on arrhythmia recurrence in obese individuals with atrial fibrillation: the CARDIO-FIT study. J Am Coll Cardiol. 2015; 66: 985-996.

46 Eaker ED, Sullivan LM, Kelly-Hayes M, et al. Anger and hostility predict the development of atrial fibrillation in men in the Framingham Offspring Study. Circulation. 2004; 109: 1267-1271.

47 Eaker ED, Sullivan LM, Kelly-Hayes M, et al. Tension and anxiety and the prediction of the 10-year incidence of coronary heart disease, atrial fibrillation, and total mortality: the Framingham Offspring Study. Psychosom Med. 2005; 67: 692-696.

48 Whang W, Davidson KW, Conen D, et al. Global psychological distress and risk of atrial fibrillation among women: the Women's Health Study. J Am Heart Assoc. 2012; 1: e001107.

49 Cheng YF, Leu HB, Su CC, et al. Association between panic disorder and risk of atrial fibrillation: a nationwide study. Psychosom Med. 2013; 75: 30-35.

50 Torén K, Schiöler L, Söderberg M, et al. The association between job strain and atrial fibrillation in Swedish men. Occup Environ Med. 2015; 72: 177-180.

51 Pathak RK, Evans M, Middeldorp ME, et al. Cost-effectiveness and clinical effectiveness of the risk factor management clinic in atrial fibrillation: the CENT study. JACC Clin Electrophysiol. 2017; 3: 436-447.

52 Pathak RK, Middeldorp ME, Meredith M, et al. Long-term effect of goal-directed weight management in an atrial fibrillation cohort. J Am Coll Cardiol. 2015; 65: 2159-2169.

53 Pathak RK, Middeldorp ME, Lau DH, et al. Aggressive risk factor reduction study for atrial fibrillation and implications for the outcome of ablation: the ARREST-AF cohort study. J Am Coll Cardiol. 2014; 64: 2222-2231.

54 Mahmood M, Lip GY. Management of atrial fibrillation: easy as ABC. Minerva Med. 2019; 110: 27-34.

55 Lip GYH. The ABC pathway: an integrated approach to improve AF management. Nat Rev Cardiol. 2017; 14: 627-628.

56 Proietti M, Romiti GF, Olshansky B, et al. Improved outcomes by integrated care of anticoagulated patients with atrial fibrillation using the simple ABC (Atrial Fibrillation Better Care) pathway. Am J Med. 2018; 131: 1359-1366.e6.

57 Pastori D, Farcomeni A, Pignatelli P, et al. ABC (Atrial fibrillation Better Care) pathway and healthcare costs in atrial fibrillation: the ATHERO-AF study. Am J Med. 2019. [Epub ahead of print].

58 Pastori D, Pignatelli P, Menichelli D, et al. Integrated care management of patients with atrial fibrillation and risk of cardiovascular events: the ABC (Atrial fibrillation Better Care) pathway in the ATHERO-AF study cohort. Mayo Clin Proc. 2018; S0025-6196(18)30891-7. [Epub ahead of print].