REVIEW ARTICLE

Revisiting the risks of incident atrial fibrillation: a narrative review. Part 1

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KEY WORDS
atrial fibrillation, prevention, risk factors

ABSTRACT
Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. Much focus has been directed towards AF prevention, given the morbidity, mortality, and financial cost to health care systems associated with this arrhythmia. There are a number of common conditions associated with the onset of AF, but not only limited to hypertension, diabetes, or smoking. As we understand the factors associated with incident AF, public health campaigns and targeted patient interventions are warranted to promote blood pressure control, glycemic control in patients with diabetes, smoking cessation to prevent AF, and associated comorbidity. In this narrative review, we consider some of the evidence linking these risk factors with AF. We additionally examine the role of risk factor modification in reducing AF burden. In Part 1 we address the evidence for hypertension, diabetes, and smoking as risk factors for incident AF.

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Received: March 3, 2019.
Accepted: April 1, 2019.
Published online: April 25, 2019.
Kardiol Pol. 2019; 77 (4): 430-436
doi:10.33963/KP.14806

Introduction Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia.[1] The lifetime risk of developing AF is almost 25% after the age of 40 years.[2,3] Approximately 2% of the United Kingdom population have AF, and it is estimated to increase to 4% by 2050.[4] Atrial fibrillation is associated with increased mortality and morbidity due to stroke, heart failure, and dementia.[1,5-8] Much focus has therefore been directed towards AF prevention, given the morbidity, mortality, and financial cost to health care systems associated with this arrhythmia.

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 discuss the relationship between AF and hypertension, diabetes, and smoking. In Part 2 (*Kardiol Pol*; May 2019 issue; in press), we will examine the evidence supporting the association between AF and alcohol consumption, increased body weight, exercise, and psychosocial factors.

Hypertension On a population-wide basis, hypertension is the most common predisposing factor for AF. The relationship between AF and blood pressure (BP) was first convincingly demonstrated by the Framingham Heart Study (FHS), in which hypertensive patients (defined as a systolic BP [SBP] of 160 mm Hg or higher, diastolic BP [DBP] of 95 mm Hg or higher, or use of antihypertensive medications) were significantly more likely to develop AF (odds ratio, 1.5 for men and 1.4 for women) over a 38-year follow-up. Similarly, the Manitoba study demonstrated a 1.42-fold increased risk of AF in hypertensive individuals over a 44-year follow-up.[9] The association between higher SBP and AF has also been noted within a shorter follow-up time of 3 years.[9,10]

The association between incremental SBP and DBP and risk of AF has been shown in a prospective, population-based study of 2014 Norwegian men who were nondiabetic and nonhypertensive at baseline. Over a 35-year follow-up, the risk of AF onset was increased 1.60-fold (95% CI, 1.15–2.21) with an SBP of 140 mm Hg or higher and 1.50-fold (95% CI, 1.10–2.03) with an SBP of 128 to 138 mm Hg, as compared with an SBP

TABLE 1 Association of hypertension with atrial fibrillation

Study	Population size, n	Population characteristics	Hypertensive population	Follow-up duration	Risk of AF with HT
Multi-Ethnic Study of Atherosclerosis[16]	5311	Mean (SD) age, 62 (10) y; men, 47%; non-white, 42.9%; black, 19.8%; Hispanic, 16.5%; Chinese–American, 6.6%	Optimal, 30%; prehypertension, 21%; hypertension, 49%	Median, 5.3 y	HR, 1.8; 95% CI, 1.004–3.2 for BP 120–139/80–89 mm Hg HR, 2.6; 95% CI, 1.6–4.4 for BP ≥140/90 mm Hg or antihypertensive medication use
WHS[12]	34 221	≥45 y (mean [SD] age, 55 [7] y); free of cardiovascular disease, cancer, or other major illnesses	SBP >130 mm Hg, 37.1% DBP >85 mm Hg, 17.2%	12.4 y	HR, 1.16; 95% CI, 1.09–1.23 for SBP, per 10-mm Hg increment HR, 1.17; 95% CI, 1.05–1.29 for DBP, per 10-mm Hg increment HR, 1.28; 95% CI, 1.00–1.63 for SBP 130–139 mm Hg HR, 1.53; 95% CI, 1.05–2.23 for DBP 85–89 mm Hg
Cohort of healthy Norwegian men[11]	2014	men aged 40 to 59 y from 5 governmental institutions in Oslo, Norway; smokers, 44%	SBP ≥140 mm Hg, 26%	Median, 30 y (up to 35 y)	HR, 1.98; 95% CI, 1.22–3.27 for SBP 128–138 mm Hg HR, 1.67; 95% CI, 1.00–2.85 for DBP 80–86 mm Hg
Cardiovascular Health Study[48]	4844	≥65 y	Hypertensive, 43.7%	3 y	HR, 1.11; 95% CI, 1.05–1.18 for SBP, per 10-mm Hg increment
Cardio-Sis[27]	1111	Nondiabetic, SBP ≥150 mm Hg	Randomized into SBP <140 mm Hg (49.7%) and <130 mm Hg (50.3%)	2 y	HR, 0.46; 95% CI, 0.22–0.98 for tight BP control group (target SBP <130 mm Hg)
FHS[14]	5331	≥35 y (median age, 57 y); women, 55%; initially free from AF,	22.75% on antihypertensive medication	Mean, 16 y (up to 20 y)	HR, 1.26; 95% CI, 1.12–1.43 for pulse pressure, per 20-mm Hg increment
LIFE[26]	8810	Mean age, 65.9 y in men and 67.9 y in women; men, 46%; white race, 92%	Pulse pressure ≥60 mm Hg, 86.5%	Mean (SD), 4.9 (0.9) y	HR, 1.39; 95% CI, 1.22–1.58 for pulse pressure, per 15.5-mm Hg increment
Multi-Ethnic Study of Atherosclerosis[15]	6630	Non-AF (6623): mean age, 62 y; men, 47% AF (307): mean age, 70 y; men, 61%	Antihypertensive therapy: non-AF, 36%; AF, 56%	Mean, 7.8 y	HR, 1.29; 95% CI, 1.05–1.59 for pulse pressure, per 17.2-mm Hg increment

Abbreviations: AF, atrial fibrillation; BP, blood pressure; DBP, diastolic blood pressure; FHS, Framingham Heart Study; HR, hazard ratio; HT, hypertension; LIFE, Losartan Intervention for Endpoint; SBP, systolic blood pressure; WHS, Women Health Study

of less than 128 mm Hg. Similarly, baseline DBP of 80 mm Hg or higher was associated with a 1.79-fold (95% CI, 1.28–2.59) increased risk of AF onset, in comparison with a DBP of less than 80 mm Hg.[11] An analogous study in women (Women's Health Study), which recruited 39 876 female health professionals aged 45 years or older without any cardiovascular disease, cancer, or other major illnesses at baseline, also showed that higher SBP and DBP were associated with increasing incidence of AF (*P* for trend <0.0001 and 0.026, respectively).[12] Notably, both of the above studies had limited generalizability to non-Caucasians. Furthermore, the majority of data considered thus far are based on a single-visit BP check.[3,9,11-15] As BP is a continuous variable, it follows that a single BP measurement may not adequately identify hypertensive individuals.

These weaknesses were addressed by the multicenter MESA study (Multi-Ethnic Study of Atherosclerosis),[16] which recruited an ethnically diverse cohort and measured BP on 3 separate occasions over a 5-year period to define a "sustained" BP category when 2 or more visits were within the same range. Both sustained prehypertension defined as a BP of 120 to 139 / 80 to 89 mm Hg and no antihypertensive medication use (hazard ratio [HR], 1.8; 95% CI, 1.004–3.2) and sustained hypertension defined as a BP of 140/90 mm Hg or higher or antihypertensive medication use at 2 consecutive visits (HR, 2.6; 95% CI, 1.6–4.4) were associated with an increased risk of AF.[16] However, one limitation of this study was that incident AF was identified through assessment of discharge summaries and inpatient Medicare data claim records, raising the possibility that patients with

TABLE 2 Antihypertensive agents and incident atrial fibrillation

Trial	Year	Study population (n) and inclusion criteria	Trial drug	AF event rate in hypertensive population, n		Odds ratio (95% CI)	Trial outcome
				Control	Intervention		
CAPPP[29]	1999	5492; age, 25–66 y; men, 54.9%; DBP ≥100 mm Hg	Captopril vs β-blockers	135	117	1.05 (0.90–1.22)	11.1/1000 patient-years in captopril group vs 10.2/1000 patient-years in control group
STOP-2[30]	1999	4401; age, 70–84 y, men, 51%; SBP ≥180 mm Hg or DBP ≥105 mm Hg or both	Conventional vs newer antihypertensive	104 (2213)	207 (4401)	1.14 (0.95–1.37)	9.58% in enalapril/lisinopril group vs 8.47% in control group
TRACE[22]	1999	790; mean age, 68 y; men, 71%; reduced LV systolic function (≤36%) following MI; sinus rhythm	1–2 mg/d trandolapril vs placebo	42	22	0.45 (0.26–0.76)	5.3% in trandolapril group vs 2.8% in placebo group
GISSI-3[25]	2001	17 749; men, 78%; MI (within 24 h of presentation), Killip class <4, no life-threatening disorder	Lisinopril + nitrates; lisinopril; nitrates; double-placebo control	385	301 in lisinopril + nitrates group; 364 in lisinopril group; 336 in nitrates group	0.76 (0.65–0.89) for lisinopril + nitrates group	6.8% in lisinopril + nitrates group; 8.2% in lisinopril group; 7.6% in nitrates group; 8.7% in double-control group
SOLVD[21]	2003	186; mean (SD) age, 56.7 (9.7) y; men, 89.8%, white race, 100%; severe LVSD	5–20 mg/d enalapril vs placebo	45	10	0.22 (0.11–0.44)	5.4% in enalapril group; 24% in placebo group
Val-HeFT[24]	2005	2205; median age, 63 y; men, 79.94%;≥18 y, at least 3-month history of HF, NYHA II–IV symptoms	Valsartan or placebo	174	113	0.63 (0.49–0.81)	5.12% in valsartan group; 7.95% in placebo group
LIFE[26]	2005	8851; hypertensive with LVH on ECG	Atenolol vs losartan	221 in atenolol	150 in losartan	0.67 (0.55–0.83)	6.8 vs 10.1/1000 person-years in losartan and atenolol groups, respectively
CHARM[23]	2006	6446; mean (SD) age, 64 (11) y; men, 78%; symptomatic HF; NYHA II–IV; LVEF ≤40%	Candesartan with a target dose of 32 mg/d vs placebo	215	177	0.812 (0.662–0.998)	5.55% in candesartan group; 6.74% in placebo group
HOPE[28]	2007	4044; ≥55 y; men, 74%; without known HF/LV systolic dysfunction	Ramipril	4291	4044	0.92 (0.68–1.24)	2.0% in ramipril group vs 2.2% in placebo group
TRANSCEND[49]	2008	2954; mean (SD) age, 66.9 (7.3) y; men, 56.7%; intolerant to ACEI	Telmisartan 80 mg/d or placebo	182 (2954)	180 (2972)	1.02 (0.82–1.26)	6.4% in telmisartan group vs 6.3% in placebo group
VALUE[50]	2008	15 245; high cardiovascular risk	Valsartan, 80–160 mg/d vs amlodipine, 5–10 mg/d	4.34% in amlodipine group	3.67% in valsartan group;	0.843 (0.713–0.997)	3.67% in valsartan group; 4.34% in amlodipine group
ALLHAT[51]	2009	39 056 (chlorthalidone, 11 695; amlodipine, 6935; lisinopril, 6702; doxazosin, 6392); men, 54.1%; age,≥55 y; at least 1 CV risk factor; AF or atrial flutter	chlorthalidone; amlodipine; lisinopril; doxazosin		244, 155, 138, and 104 in chlorthalidone, amlodipine, lisinopril, and doxazosin groups, respectively	Chlorthalidone, 1.00; amlodipine, 1.083 (0.87–1.34); lisinopril, 0.939 (0.74–1.18); doxazosin, 1.326	20.9, 22.4, 20.6, and 16.3/1000 participants in chlorthalidone, amlodipine, lisinopril, and doxazosin groups, respectively

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ALLHAT, Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; CAPPP, CAPtopril Prevention Project; CHARM, Candesartan in Heart failure: assessment of Reduction in Mortality and morbidity; ECG, electrocardiogram; GISSI-3, Gruppo Italiano per lo studio della sopravvivenza nell'Infarto miocardico; HF, heart failure; HOPE, Heart Outcomes Prevention Evaluation Study; LV, left ventricular; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; LVSD, left ventricular systolic dysfunction; MI, myocardial infarction; NYHA, New York Heart Association; SOLVD, Studies of Left Ventricular dysfunction; STOP-2, Swedish Trial in Old; TRACE, TRAndolapril Cardiac Evaluation; TRANSCEND, Telmisartan Randomised AssessmeNt Study in ACE iNtolerant subjects with cardiovascular Disease; Val-HeFT, Valsartan Heart Failure Trial; VALUE, Valsartan Antihypertensive Long-term Use Evaluation; others, see TABLE 1

TABLE 3 Studies relating to diabetes and incident atrial fibrillation

Study	Population size, n	Population characteristics	Diabetic population	Follow-up duration	Risk of AF with DM
Group Health in United States[35]	1410 newly recognized AF cases and 2203 controls	Age, 30–84 y; case-control study from Group Health cohort; median age, 74 and 68 y in case and control groups, respectively; men, 35.4% and 45.2% in case and control groups, respectively; white race, 93.4% and 88.6% in case and control groups, respectively	Treated DM, 17.9% and 14.1% in case and control groups, respectively; patients with untreated DM excluded from analysis	3 y: 10/1/2001–12/31/2004	OR, 1.07; 95% CI, 0.75–1.51 for treated diabetes <5 y OR, 1.51; 95% CI, 1.05–2.16 for >5 but ≤10 y OR, 1.64; 95% CI, 1.22–2.20 for >10 y OR, 1.03; 95% CI: 1.01–1.06 for each year treated diabetes duration
ARIC[33]	13 025	Mean (SD) age, 57 (5.7) y; men, 44.1%; African-American, 22.9%	pre-diabetes, 51.4%; diabetes, 14.9%	14.5 y: 1990–2007	HR, 1.13; 95% CI, 1.07–1.20 in those with diabetesHR, 1.05; 95% CI, 0.96–1.15 in those without diabetes
NAVIGATOR[34]	8943 patients with impaired glucose tolerance	Median (Q1, Q3) age at screening, 63 (58, 68) y; men, 48.7%; white race, 82.9%	Median HbA_{1c}, 6%	6.5 y	Adjusted HR, 1.33; 95% CI, 1.11–1.59 for FBG (per 1-mmol/l increase)
HS[52]	34 720	Mean age in patients without T2DM at baseline, 52.8 (48.9–58.7) y; mean age in patients with T2DM at baseline, 55.5 (50.0–62.1); all female health professionals; age, ≥45 y; no cardiovascular risk, cancer, or AF	T2DM at baseline, 2.7%	16.4 y: 1993–2011	HR, 1.37; 95% CI, 1.03–1.83 for DM in multivariate--adjusted model HR, 1.09; 95% CI, 0.93–1.27 for DM and 1% rise in HbA_{1c} level
ACCORD[40]	10 082	Mean (SD) age, 62.2 (6.8) y; men, 61.4%; white race, 64.9%; patients with DM; HbA_{1c} level ≥7.5; age range, 40–79 y; at least 1 additional cardiovascular risk factor	Intensive therapy targeting HbA_{1c} <6.0%; standard therapy targeting HbA_{1c} 7.0%–7.9%	Median, 4.68 y	Incident rate of AF: 5.9/1000 person-years in the intensive-therapy group; 6.37/1000 person-years in the standard-therapy group (P = 0.52)
VALUE[32]	15 245	Mean age across group, 65–67 y; men, 57%, Caucasian race, 91%	3 groups: nondiabetic, diabetic at baseline, diabetes developed during study	Mean, 4.2 y	Adjustable multivariate HR, 1.38; 95% CI, 1.05–1.80 for new-onset AF in new-onset DMAdjustable multivariate HR, 1.66; 95% CI, 1.13–2.44 for persistent AF in new-onset DM
Niigata Preventive medicine study[36]	28 449	Japanese community; mean (SD) age, 59.2 (11) y; men, 34%, diabetics, 12%	Metabolic vs no metabolic syndrome as per NCEP-ATP III and AHA-NHLBI	Mean, 4.5 y	Metabolic syndrome: HR, 1.44; 95% CI, 1.09–1.90 for impaired glucose tolerance (NCEP-ATP III)HR, 1.35; 95% CI, 1.06–1.73 for impaired glucose tolerance (AHA-NHLBI)

Abbreviations: ACCORD, Action to Control Cardiovascular Risk in Diabetes Study; AHA-NHLBI, American Heart Association – National Heart, Lung and Blood Institute; ARIC, Atherosclerosis Risk in Communities; DM, diabetes mellitus; HbA_{1c}, glycated hemoglobin A_{1c}, NAVIGATOR, Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research, NCEP-ATP III, National Cholesterol Education Program – Adult Treatment Panel III; T2DM, type 2 diabetes mellitus; others, see TABLES 1 and 2

paroxysmal AF without clinical symptomatology were not accounted for in the analysis.

In addition, individual components of BP, including SBP, pulse pressure, and even arterial pressure, have been evaluated regarding the risk of AF. The Cardiovascular Health Study demonstrated that risk of incident AF increased with every 10-mm Hg rise in SBP (HR, 1.11; 95% CI, 1.05–1.18), and it was marginally lower if no cardiovascular risk factors were present (HR, 1.06; 95% CI, 0.98–1.15) compared with the presence of cardiovascular risk factors (HR, 1.14; 95% CI, 1.05–1.23).[10] One FHS offspring study report has noted that pulse pressure (HR, 1.26 per 20-mm Hg increment; 95% CI, 1.12–1.43; P <0.001) but not mean arterial pressure (P = 0.39) led to an increased risk of AF in a model adjusted for age, sex, and clinical risk factors

TABLE 4 Smoking and incident atrial fibrillation

Study	Study period	Follow-up, y	Sample size, n	Population characteristics	AF cases, n	Group studied	Adjusted HR (95% CI)	Conclusion
FHS[13]	1968–1971, 1981–1984, 1971–1975, 1984–1987	38	4764	Mean age, 60.9 y (range, 45 to 95 y); men, 45%	457	Current smokers	Men, 1.00 (0.7–1.4); women, 1.5 (1.0–2.2)	Smoking has no significant relationship with AF.
Shinken Database[41]	2004–2012	Mean (SD), 2 (2.1)	15 221	Men, 59.2%; mean age in smokers, 57 y; hospital-based cohort in Japan	190	Current smokers	1.81 (1.17–2.79)	Smoking is independently associated with new-onset AF. In current smokers, there was no significant difference observed by total tobacco consumption. Highlights importance of Tobacco discontinuation.
						Current smoker Brinkmann index ≥800	1.69 (1.05–2.70)	
ARIC[43]	1987–2002	13.1	15 329	Age range, 45–64 y; mean (SD) age, 54 (5.8) y; men, 44.8%; black race, 30.3%, 19.4%, and 29.5% in current, former, and never smokers, respectively	876	Former smokers	1.32 (1.10–1.57)	Smoking was associated with the incidence of AF.Current smoking is associated with more than a 2-fold increased risk of AF.In addition, a trend toward a lower incidence of AF appeared among smokers who quit compared to continued smokers.
						Current smokers	2.05 (1.71–2.47)	
						Ever smoker	1.58 (1.35–1.85)	
						>675 cigarette-years	2.10 (1.74–2.53)	
						Discontinuation of smoking vs continued smoking	0.88 (0.65–1.17)	
Rotterdam Study[44]	1990–1993	7.2	5668	Age ≥55 y; women among never-smokers, 90%; among current smokers, 52.9%; and among former smokers, 45.8%	371	Current smokers	1.51 (1.07–2.12)	Current and former smoking of cigarettes is associated with increased risk of atrial fibrillation.
						Former smokers	1.49 (1.14–1.97)	

Abbreviations: see TABLES 1 and 3

for AF, including body mass index, smoking, valvular disease, and diabetes.[14] Moreover, a visit-to-visit variability in SBP was also predictive of major adverse outcomes including ischemic stroke and major bleeding (P <0.001 for both).[17,18]

There are several explanations for the association between elevated BP and AF, including structural changes such as an increase in the left atrial diameter[19] and arterial stiffness.[14,19] It is also plausible that enlargement of the left atrium secondary to hypertension may result in pulmonary vein trunk dilation, which subsequently plays a role in the genesis and maintenance of AF.[20] Elevated BP is also linked to conditions that predispose to AF development, such as advanced age, diabetes, and coronary heart disease.

The influence of antihypertensive medications on incident AF has been assessed in a variety of randomized controlled trials; however, the results have been mixed. Some trials clearly demonstrate a significant reduction in incident AF event rates, for example, with enalapril treatment in left ventricular dysfunction,[21] trandolapril treatment post myocardial infarction,[22] valsartan and candesartan in heart failure,[23,24] and lisinopril with nitrates post myocardial infarction.[25] The LIFE trial[26] (Losartan Intervention for Endpoint) has additionally reported fewer AF events with losartan therapy compared with atenolol in hypertensive patients with electrocardiographic evidence of left ventricular hypertrophy. Furthermore, Verdecchia et al[27] have shown that the use of antihypertensive agents to achieve tight BP control with a target of less than 130 mm Hg is associated with a reduced incidence of AF compared with lenient BP control with a target of less than 140 mm Hg (HR, 0.46; 95% CI, 0.22–0.98; P = 0.044). In contrast, other trials have failed to show the change in AF event rates when ramipril was compared with placebo,[28] captopril with β-blocker and diuretics,[29] and conventional with newer antihypertensives.[30]

In summary, hypertension is associated with an increased risk (up to 2-fold) of incident AF, irrespective of sex or ethnicity. This relationship was consistent not only with SBP but also with pulse pressure. Moreover, this relationship is linear such that there is a 11% to 17% increased risk of AF with every 10-mm Hg rise in BP. The risk of incident AF falls with stricter BP control (up to 50% reduced risk), which similarly demonstrates this linear relationship. Therefore, adequate assessment of at-risk patients and tight BP control are recommended to reduce the risk of AF.

Diabetes mellitus and metabolic syndrome

Various epidemiological studies have investigated the relationship between diabetes mellitus and incident AF. The FHS was one of the earliest studies to recognize diabetes as an independent risk factor for AF,[13] while the Renfrew/Paisley study first associated elevated blood glucose

with a higher incidence of AF.[10,31] A subgroup analysis of the VALUE Trial[32] (an international multicenter trial to assess the incidence of cardiac events in hypertensive patients taking valsartan or amlodipine) similarly showed that patients who developed diabetes during the follow-up of 4.2 years had a higher risk of incident AF (relative risk [RR], 1.38; 95% CI, 1.05–1.80) and were more likely to have persistent AF (HR, 1.66; 95% CI, 1.13–2.44).

A number of studies have sought to investigate the relationship between glycemic control and the incidence of AF. For instance, the ARIC Study[33] (Atherosclerosis Risk in Communities) showed a linear relationship between glycated hemoglobin A_{1c} (HbA_{1c}) levels and AF incidence (HR, 1.13; 95% CI, 1.07–1.20 per 1% rise). The NAVIGATOR study[34] showed that for a 1.0-mmol rise in fasting glucose levels there was a 33% increase in the risk of AF (HR, 1.33; 95% CI, 1.11–1.59). A community-based case control study known as Group Health[35] further revealed that for each additional year of diabetes the risk of developing AF was 3% higher, suggesting that the longer duration of diabetes increases the risk of AF. Moreover, the Niigata Preventive Medicine Study[36] not only demonstrated that impaired fasting glucose was associated with a higher incidence of AF (HR, 1.35; 95% CI, 1.06–1.73; $P = 0.01$), but also showed that individuals with metabolic syndrome (defined by National Cholesterol Education Program Third Adult Treatment Panel criteria) had a higher risk of AF onset (HR, 1.88; $P = 0.001$).

A number of hypotheses have been postulated to explain the link between diabetes and AF, including diabetic microangiopathy, abnormal sympathetic tone,[37] diabetic cardiomyopathy,[38,39] and metabolic fluctuation.[37] It is also pertinent to consider whether adequate glycemic control may reduce the risk of AF. Unfortunately, data from 10 082 diabetic patients from the ACCORD trial[40] (Action to Control Cardiovascular Risk in Diabetes) showed that intensive glycemic control (HbA_{1c} <6.0%) compared with standard glycemic control (HbA_{1c}, 7.0%–7.9%) led to no significant difference in the incidence of AF (5.9 per 1000 patient-years and 6.37 per 1000 patient-years, respectively, $P = 0.52$).

In summary, diabetes increases the risk (11%–37%) of incident AF. This risk includes prediabetes, metabolic syndrome, and treated diabetes. The risk of AF increases with poor glycemic control and longer duration of diabetes. Intensive glycemic control does not offer significant advantages at least in the short term.

Smoking A number of studies have explored the relationship between smoking and development of AF, in particular, the influence of duration and quantity of tobacco on AF risk.

For instance, an analysis of 15 221 patients diagnosed with AF from the Shinken database revealed that smokers were more likely to develop AF, with an incidence rate of 9.0 and 5.0 per 1000 patient-years for smokers and nonsmokers, respectively.[41,42] There was additionally no difference in the risk of AF between men and women ($P = 0.195$). The Manitoba follow-up study similarly demonstrated an increased risk of AF in smokers (RR, 1.37; 95% CI, 1.00–1.87).[9]

Furthermore, the ARIC study[43] showed that both current (HR, 2.05; 95% CI, 1.71–2.47) and former smokers (HR, 1.32; 95% CI, 1.10–1.57) had an increased risk of AF, as compared with individuals who had never smoked. Those with the longest smoking history (>675 cigarette-years) had the highest risk of AF (RR, 2.10; 95% CI, 1.74–2.53) compared with nonsmokers. Those who quit smoking had a marginally lower risk of AF (HR, 0.88; 95% CI, 0.65–1.17), as compared with current smokers, although the difference was nonsignificant ($P = 0.38$).[43] The Rotterdam study similarly noted that current (RR, 1.51; 95% CI, 1.07–2.12) and former (RR, 1.49; 95% CI, 1.14–1.97) smokers had an increased risk of incident AF.[44]

What are the potential mechanisms? Smoking leads to an increased risk of AF by inducing oxidative stress,[45,46] inflammation,[45,46] and atrial fibrosis.[46,47] Further research to consider the threshold at which these pathophysiological changes are reversible to return AF risk to baseline are warranted.

In summary, smoking is not only a risk factor for AF but also for conditions that can predispose to heart failure and subsequent development of AF. Discontinuation of smoking may reduce the further risks of AF. More research is recommended to evaluate the impact of e-cigarettes and passive smoking on AF, as well as the impact of smoking cessation on reducing the risk of stroke, myocardial infarction, chronic kidney disease, and all-cause mortality.

Conclusion It is clear that hypertension, diabetes, and smoking predispose to the onset of AF, which is particularly important when considering that these risk factors are modifiable. Thus, strategies to promote BP and glycemic control as well as smoking cessation must shape public health strategy.

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 1. Kardiol Pol. 2019; 77: 430-436. doi:10.33963/KP.14806

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