# Cigarette Smoking, Cessation, and Risk of Heart Failure With Preserved and Reduced Ejection Fraction

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## ABSTRACT

**BACKGROUND** Smoking is well-recognized as a risk factor for heart failure (HF). However, few studies have evaluated the prospective association of cigarette smoking and smoking cessation with heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF) as distinct phenotypes.

**OBJECTIVES** The aim of this study was to quantify the association of cigarette smoking and smoking cessation with the incidence of HFpEF and HFrEF.

**METHODS** In 9,345 ARIC (Atherosclerosis Risk In Communities) study White and Black participants without history of HF at baseline in 2005 (age range 61-81 years), we quantified the associations of several established cigarette smoking parameters (smoking status, pack-years, intensity, duration, and years since cessation) with physician-adjudicated incident acute decompensated HF using multivariable Cox models.

**RESULTS** Over a median follow-up of 13.0 years, there were 1,215 incident HF cases. Compared with never smokers, current cigarette smoking was similarly associated with HFpEF and HFrEF, with adjusted HRs ~2. There was a dose-response relationship for pack-years of smoking and HF. A more extended period of smoking cessation was associated with a lower risk of HF, but significantly elevated risk persisted up to a few decades for HFpEF and HFrEF.

**CONCLUSIONS** All cigarette smoking parameters consistently showed significant and similar associations with HFpEF and HFrEF. Smoking cessation significantly reduced the risk of HF, but excess HF risk persisted for a few decades. Our results strengthened the evidence that smoking is an important modifiable risk factor for HF and highlighted the importance of smoking prevention and cessation for the prevention of HF, including HFpEF.
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Heart failure (HF) affects at least 26 million people worldwide.[1] Around 6.2 million U.S. adults are estimated to have HF.[2] This estimate is projected to exceed 8 million in 2030, partially because of the aging population.[2] Although much improved in the last few decades, the prognosis of HF is still devastating, with a 1-year mortality of ~30% after its diagnosis.[2] Preventive approaches are crucial for HF, especially for heart failure with preserved ejection fraction (HFpEF), because HFpEF lacks specific treatment with robust evidence to date.[3] Notably, the prevalence of HFpEF is increasing relative to heart failure with reduced ejection fraction (HFrEF).[3]

Smoking is considered a major modifiable risk factor for HF, accounting for 14% of excess risk of incident HF.[4] Recent systematic reviews showed an increased risk of HF among current and former

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smokers.[5,6] Nonetheless, only a few studies have evaluated the associations of smoking with HFrEF and HFpEF separately and reported conflicting results.[7-11] For example, results from the MESA (Multi-Ethnic Study of Atherosclerosis) and the Women's Health Initiative study found that current (vs never or noncurrent) cigarette smoking was significantly associated with HFrEF and HFpEF.[7,9] However, Ho et al[11] pooled data from 4 community-based prospective cohorts and found that current smoking was significantly associated with HFrEF but not HFpEF. In addition, few studies explored smoking intensity, duration, and pack-years in terms of HF risk[9,12] and how long the impact of smoking lasts in former smokers for 2 phenotypes of HF is unknown.

Therefore, using data from a community-based prospective cohort, the ARIC (Atherosclerosis Risk In Communities) study, we comprehensively quantified the association of cigarette smoking and smoking cessation with incident HF, overall and with its 2 phenotypes, HFrEF and HFpEF. In addition, the longitudinal data in ARIC allowed us to evaluate the effect of long-term smoking cessation over 30 years.

## METHODS

**STUDY POPULATION.** The ARIC study enrolled 15,792 participants aged 45-64 years from 4 U.S. communities. The first clinic examination (visit 1) took place from 1987-1989, with 3 short-term clinic examinations (visits 2-4) happening in 1990-1992, 1993-1995, and 1996-1998, respectively. Subsequent visits 5, 6, and 7 took place during 2011-2013, 2016-2017, and 2018-2019, respectively.[13] In addition, phone interviews were conducted annually from visit 1 to 2011 and semiannually after that. The ARIC study was approved by the Institutional Review Board of each participating center, and informed consent was obtained from each participant.

For this specific study, we used January 1, 2005, as the baseline, because the adjudication for potential HF cases in the ARIC study started at the beginning of 2005. This approach allowed us to maximize the number of adjudicated HF events and link them to cigarette smoking status using smoking data from phone interviews and study visits closest to January 1, 2005 (Supplemental Figure 1). A total of 10,407 participants were alive and not lost to follow-up at the beginning of 2005. We excluded participants who had prior HF (n = 877), which was defined as the Gothenburg stage 3, a status with dyspnea caused by cardiac causes and under treatment with digitalis or loop diuretics, or incident HF (hospitalization with International Classification of Diseases code beginning with "428") between visit 1 and December 31, 2004. We also excluded those with missing variables of interest (n = 275) (Supplemental Figure 2). The final study sample included 9,345 participants.

**CIGARETTE SMOKING MEASURES.** Our exposure of interest was cigarette smoking. We did not explore cigars, pipes, or secondhand smoking because of the lack of information around the baseline of this study. The ARIC study assessed cigarette smoking status (current, former, never smoker) at each visit and annual/semiannual phone interview. Smoking duration was calculated based on participants' cumulative years of smoking before visit 1 plus the years smoked during the follow-up. Smoking intensity was assessed at study visits 1-4. Then, we calculated pack-years of smoking as the average number of cigarettes/d divided by 20 (converting to packs/d) times the duration of smoking in years.

Years since cessation in former smokers was calculated as baseline age minus the recalled age of cessation plus the cumulative years of cessation during follow-up. Specifically, if the former smoker (at baseline or during follow-up) responded "no" to the question "Do you now smoke cigarettes," years since cessation was accumulated for the time between 2 contacts. If current smokers transitioned to noncurrent smokers, the midpoint of data collection dates was assigned as cessation time. Once never or former smokers transitioned to current smokers, they were categorized as current smokers until a subsequent visit or phone interview reporting noncurrent smoking and then started to cumulate quitting years from 0.

**COVARIATES.** Covariates were collected during study visits and phone interviews (Supplemental Figure 1). Age was calculated using January 1, 2005, minus date of birth. Sex, race, and educational level were self-reported at visit 1. Education was categorized as advanced (at least some college), intermediate (high school or vocational school), and no or basic (less than high school). Drinking status was self-reported at visit 4. Weight and height were measured at visit 4, and body mass index (BMI) was calculated as body weight (in kilograms) over height (in meters) squared. Seated blood pressure was measured twice after 5 minutes of rest using a random-zero sphygmomanometer at visit 4, and the average of the 2 readings was recorded. Total cholesterol and high-density lipoprotein (HDL)

**ABBREVIATIONS AND ACRONYMS**

**BMI** = body mass index

**CHD** = coronary heart disease

**eGFR** = estimated glomerular filtration rate

**HDL** = high-density lipoprotein

**HF** = heart failure

**HFpEF** = heart failure with preserved ejection fraction

**HFrEF** = heart failure with reduced ejection fraction

**LVEF** = left ventricular ejection fraction

**TABLE 1 Baseline Characteristics by Cigarette Smoking Status (N = 9,345)**

| | Cigarette Smoking Status | | |
|---|---|---|---|
| | Never Smokers (n = 3,975) | Former Smokers (n = 4,547) | Current Smokers (n = 823) |
| Age, y | 70.5 ± 5.7 | 70.4 ± 5.6 | 68.7 ± 5.4 |
| Men | 1149 (28.9) | 2462 (54.1) | 376 (45.7) |
| Black | 933 (23.5) | 812 (17.9) | 196 (23.8) |
| Body mass index, kg/m$^2$ | 28.9 ± 5.6 | 28.6 ± 5.2 | 26.7 ± 4.9 |
| Education level | | | |
| No or basic | 649 (16.3) | 735 (16.2) | 201 (24.4) |
| Intermediate | 1,715 (43.1) | 1,917 (42.2) | 350 (42.5) |
| Advanced | 1,611 (40.5) | 1,895 (41.7) | 272 (33.0) |
| Drinking status | | | |
| Current drinker | 1,611 (40.5) | 2,705 (59.5) | 469 (57.0) |
| Former drinker | 938 (23.6) | 1,446 (31.8) | 251 (30.5) |
| Never drinker | 1,426 (35.9) | 396 (8.7) | 103 (12.5) |
| Systolic blood pressure, mm Hg | 127.4 ± 18.3 | 126.3 ± 18.1 | 124.3 ± 19.7 |
| Total cholesterol, mmol/L | 5.3 ± 1.0 | 5.2 ± 0.9 | 5.2 ± 1.0 |
| HDL cholesterol, mmol/L | 1.4 ± 0.4 | 1.3 ± 0.4 | 1.2 ± 0.4 |
| eGFR, mL/min/1.73 m$^2$ | 86.4 ± 15.4 | 86.9 ± 14.6 | 91.1 ± 15.3 |
| Antihypertensive medication | 2,154 (54.2) | 2,427 (53.4) | 404 (49.1) |
| Cholesterol-lowering medication | 1,357 (34.1) | 1,790 (39.4) | 266 (32.3) |
| Diabetes | 883 (22.2) | 1,084 (23.8) | 177 (21.5) |
| Prevalent coronary heart disease | 202 (5.1) | 484 (10.6) | 82 (10.0) |

Values are mean ± SD or n (%).
eGFR = estimated glomerular filtration rate; HDL = high-density lipoprotein.

cholesterol were determined using enzymatic methods at visit 4. Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration creatinine equation at visit 4.[14] Antihypertensive and cholesterol-lowering medication use was self-reported at an annual phone interview in 2004. Prevalent diabetes mellitus was defined as fasting glucose ≥7.0 mmol/L or nonfasting glucose ≥11.1 mmol/L at study visits, and self-reported physician diagnosis of diabetes or the use of glucose-lowering medications at study visits or phone interviews before December 31, 2004. History of coronary heart disease (CHD) was defined by self-reported history of myocardial infarction or prior coronary reperfusion procedure and electrocardiogram evidence of myocardial infarction at visit 1 and adjudicated events from visit 1 through December 31, 2004. Incident CHD events during follow-up were defined as adjudicated definite or probable myocardial infarction or fatal CHD.

**OUTCOMES.** The ARIC study abstracted medical records for cohort members hospitalized with HF from 2005, as previously described.[15,16] Hospitalizations were adjudicated by a physician panel and classified as definite acute decompensated HF, probable acute decompensated HF, stable chronic HF, not HF, or unclassifiable. We included definite and probable acute decompensated HF as the outcome. Based on left ventricular ejection fraction (LVEF) available in hospitalization records, HF was classified as HFrEF or HFpEF (LVEF <50% or ≥50%, respectively).[17,18] Participants were followed until an HF event, date of death, date of the last contact, or December 31, 2019, whichever came first.

**STATISTICAL ANALYSES.** We compared baseline characteristics of the study population according to cigarette smoking status (current, former, and never) at baseline. Never smoker was used as the reference group in most analyses.

Cox proportional hazards models were used to quantify the associations between cigarette smoking measures and incident HF (overall HF, HFpEF, and HFrEF). The proportional hazards assumption was verified using log-log plots. Based on the distribution, pack-years was modeled continuously (per 10 pack-years increment) and categorically (<10, 10-<25, 25-<40, and ≥40 pack-years among current and former smokers). Duration of smoking was largely evenly categorized as <20 and ≥20 years among former smokers and <40 and ≥40 years among current smokers. Intensity of smoking was classified as <1 and ≥1 pack/d among former and current smokers. We adjusted for the following time-fixed covariates: age, race, sex, education level, BMI, total cholesterol, HDL cholesterol, drinking status, systolic blood pressure, blood pressure-lowering medication use, cholesterol-lowering medication use, eGFR, diabetes, and CHD.

Years since cessation in former smokers (<10, 10-<20, 20-<30, and ≥30 years) were explored as a time-varying variable, with each participant contributing person-time and events to separate time bins. Time-varying covariates (age, BMI, total cholesterol, HDL cholesterol, drinking status, systolic blood pressure, blood pressure-lowering medication use, cholesterol-lowering medication use, eGFR, diabetes, prevalent and incident CHD) were used for this analysis (Supplemental Figure 1). In the case of missing data in either visits or phone interviews, we carried forward the relevant data from a prior visit or phone interview until any different information was subsequently available.

We conducted a few sensitivity analyses. To account for the potential impact for competing risk of death, we ran Fine and Gray's proportional subhazards models.[19] We used the likelihood ratio test to assess potential interaction by key demographic and

clinical factors (eg, age, sex, race, alcohol use, hypertension, diabetes, and CHD) at baseline. We conducted statistical analyses using Stata SE version 16 (Stata Corp), and a $P$ value of <0.05 was considered statistically significant.

## RESULTS

**BASELINE CHARACTERISTICS.** The mean age of 9,345 participants was 70.4 ± 5.7 years, with 57.3% women and 20.8% Black participants. There were 823 (8.8%) current smokers, 4,547 (48.7%) former smokers, and 3,975 (42.5%) never smokers. Compared with never smokers, current smokers were more likely to be younger, men, less educated, and current drinkers (Table 1). Current smokers also had a lower BMI and blood pressure, a higher eGFR, a lower prevalence of antihypertensive medication and cholesterol-lowering medication use, but a higher prevalence of CHD. Former smokers had the highest proportion of men, the lowest proportion of Black participants, and the highest prevalence of cholesterol-lowering medication use and CHD.

**CIGARETTE SMOKING AND THE RISK OF INCIDENT HF.** Over a median follow-up of 13.0 years, there were 1,215 cases of incident acute decompensated HF, including 555 cases of HFpEF, 492 cases of HFrEF, and 168 HF cases with unknown LVEF. The crude incidence rate of HF was 11.3 per 1,000 person-years. The age-, sex-, and race-adjusted incidence rate per 1,000 person-years for HF was 9.7 (95% CI: 8.7-10.6) for never smokers, 13.5 (95% CI: 12.5-14.6) for former smokers, and 20.1 (95% CI: 16.7-23.5) for current smokers (Supplemental Table 1). The adjusted incidence rate was largely similar for HFpEF and HFrEF within each smoking category. Compared with never smokers, the HR for overall HF was 2.36 (95% CI: 1.92-2.90) in current smokers and 1.36 (95% CI: 1.19-1.55) in former smokers (Table 2). The associations were generally similar for HFpEF and HFrEF (eg, HRs for current smokers 2.28 [95% CI: 1.67-3.10] and 2.16 [95% CI: 1.55-3.00], respectively). The associations were modestly attenuated in competing risk models but remained significant (eg, sub-HRs for current smokers 1.60 [95% CI: 1.17-2.18] and 1.51 [95% CI: 1.08-2.10], respectively) (Supplemental Table 2).

Pack-years of smoking showed a graded association with HF after adjusting for potential confounding variables (Table 3). Compared with never smokers, those who smoked for over 25 pack-years had ~2-fold increased risk for HF. Smoking for 10-<25 pack-years was associated with a borderline increased risk of overall HF (HR: 1.19; 95% CI: 0.99-1.44). Smoking for <10 pack-years was not necessarily associated with an elevated risk of overall HF. The analyses for HFpEF and HFrEF revealed similar results. When we modeled pack-years of smoking continuously, the HRs per 10 pack-years increment were 1.16 (95% CI: 1.12-1.20) and 1.09 (95% CI: 1.05-1.13) for HFpEF and HFrEF, respectively. We observed a similar pattern in competing risk models (Supplemental Table 3). There were generally consistent results across subgroups (eg, sex, race, history of CHD) without significant interactions (Supplemental Figure 3).

A similar dose-response relationship was detected when we categorized pack-years in former and current smokers separately (Supplemental Table 4). Likewise, smoking intensity and duration showed graded associations with overall HF, HFpEF, and HFrEF (Supplemental Table 4).

**CIGARETTE SMOKING CESSATION AND THE RISK OF INCIDENT HF.** The decreasing risk of HF with a longer duration of smoking cessation was depicted in Figure 1. However, compared with never smokers, a significantly elevated risk of HF persisted up to 20-<30 years after smoking cessation (HR: 1.34; 95% CI: 1.07-1.67). This pattern was seen when we analyzed HFpEF and HFrEF separately, although the HR for HFrEF in smoking cessation 20-<30 years was not statistically significant (Central Illustration). Long-term smoking cessation over 30 years showed a

**TABLE 2 Adjusted HRs (95% CIs) for Incident HF by Cigarette Smoking Status**

| | Cigarette Smoking Status | | |
|---|---|---|---|
| | Never Smokers (n = 3,975) | Former Smokers (n = 4,547) | Current Smokers (n = 823) |
| HF | | | |
| Events | 425 | 658 | 132 |
| Adjusted HR | 1.00 (reference) | **1.36 (1.19-1.55)** | **2.36 (1.92-2.90)** |
| HFpEF | | | |
| Events | 213 | 285 | 57 |
| Adjusted HR | 1.00 (reference) | **1.31 (1.08-1.59)** | **2.28 (1.67-3.10)** |
| HFrEF | | | |
| Events | 158 | 281 | 53 |
| Adjusted HR | 1.00 (reference) | **1.36 (1.10-1.68)** | **2.16 (1.55-3.00)** |

Model adjusted for age (y), race (Black, White), sex (male, female), education level, body mass index, total cholesterol, high-density lipoprotein cholesterol, drinking status (current, former, never), systolic blood pressure, blood pressure-lowering medication use, cholesterol-lowering medication use, kidney function, diabetes, and prevalent coronary heart disease. All variables are time-fixed variables. **Bold** indicates statistical significance.

HF = heart failure; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction.

**TABLE 3** Adjusted HRs (95% CIs) for Incident HF by Pack-Years of Smoking

| | | Pack-Years of Smoking | | | | |
|---|---|---|---|---|---|---|
| | Never Smokers (n = 3,975) | <10 (n = 1,742) | 10-<25 (n = 1,318) | 25-<40 (n = 1,025) | ≥40 (n = 1,285) | Per 10 Pack-Years (n = 9,345) |
| HF | | | | | | |
| Events | 425 | 186 | 161 | 186 | 257 | 1,215 |
| Adjusted HR | 1.00 (reference) | 1.03 (0.86-1.23) | 1.19 (0.99-1.44) | **1.96 (1.63-2.36)** | **2.35 (1.98-2.78)** | **1.14 (1.11-1.16)** |
| HFpEF | | | | | | |
| Events | 213 | 77 | 76 | 77 | 112 | 555 |
| Adjusted HR | 1.00 (reference) | 0.89 (0.68-1.17) | 1.25 (0.95-1.64) | **1.88 (1.42-2.47)** | **2.51 (1.95-3.22)** | **1.16 (1.12-1.20)** |
| HFrEF | | | | | | |
| Events | 158 | 88 | 66 | 82 | 98 | 492 |
| Adjusted HR | 1.00 (reference) | 1.19 (0.91-1.56) | 1.13 (0.83-1.52) | **1.94 (1.46-2.58)** | **1.93 (1.47-2.55)** | **1.09 (1.05-1.13)** |

Model adjusted for age (y), race (Black, White), sex (male, female), education level, body mass index, total cholesterol, high-density lipoprotein cholesterol, drinking status (current, former, never), systolic blood pressure, blood pressure–lowering medication use, cholesterol-lowering medication use, kidney function, diabetes, and prevalent coronary heart disease. All variables are time-fixed variables. **Bold** indicates statistical significance.

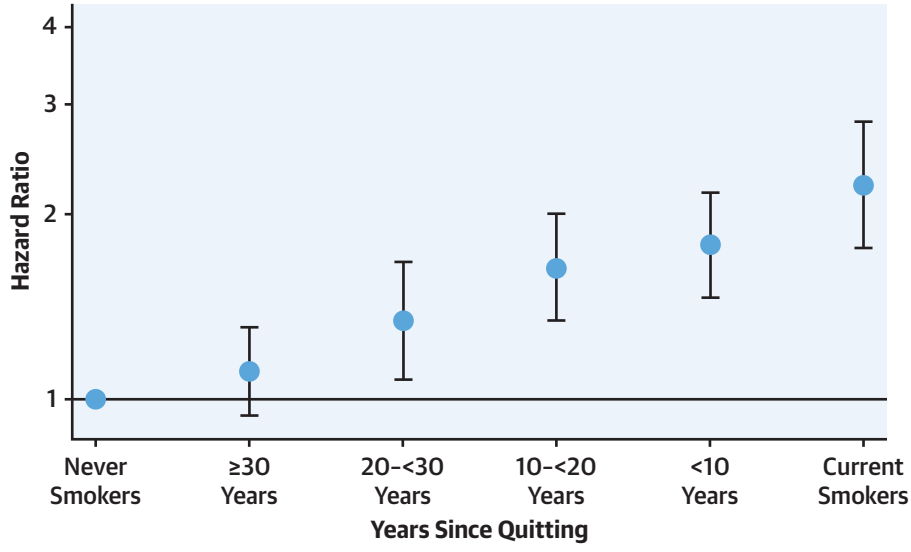
Abbreviations as in Table 2.

similar risk with never smokers for overall HF and the 2 HF phenotypes. When we used current smokers as the reference group, smoking cessation for <10 years had an HR of 0.85 (95% CI: 0.56-1.27) for HFpEF and 0.63 (95% CI: 0.42-0.95) for HFrEF (Supplemental Table 5). There was an approximately 50% lower risk for both phenotypes of HF among those who remained abstinent for over 30 years compared with current smokers. Competing risk analysis yielded similar results (Supplemental Table 6).

## DISCUSSION

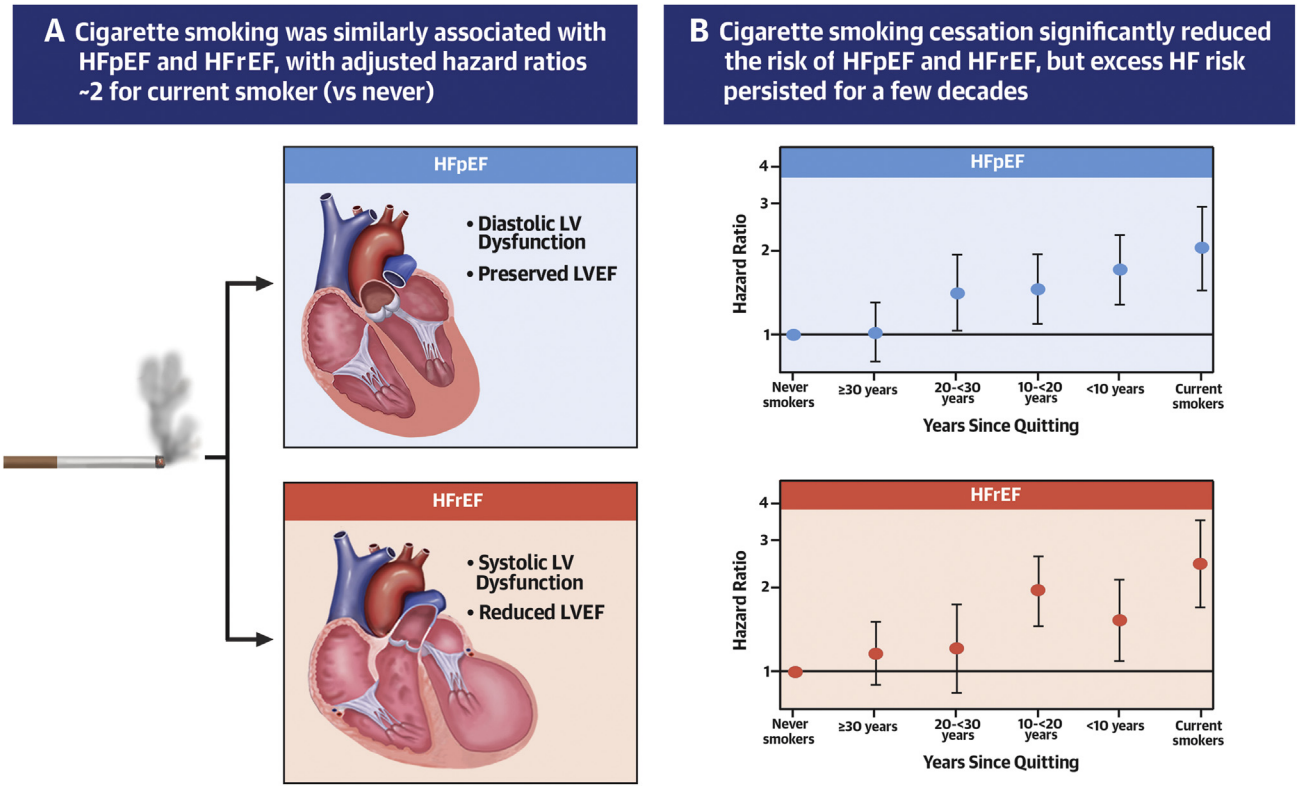
All cigarette smoking measures showed a robust dose-response relationship with incident acute decompensated HF in this large biracial community-based cohort, with a similar association for HFpEF and HFrEF. Those who smoked for ≥25 pack-years had ~2-fold increased risk for HF compared with never smokers. The associations were consistent regardless of demographic and clinical factors such as

**FIGURE 1** Adjusted HR for Incident Heart Failure by Years Since Cessation




Longer duration of smoking cessation was associated with reduced risk of incident heart failure. Results shown are from Cox model adjusted for age (years), race (Black, White), sex (male, female), education level, body mass index, total cholesterol, high-density lipoprotein cholesterol, drinking status (current, former, never), systolic blood pressure, blood pressure–lowering medication use, cholesterol-lowering medication use, kidney function, diabetes, and prevalent and incident coronary heart disease. All variables are time-varying variables.

**CENTRAL ILLUSTRATION** **Smoking and its Cessation Associated With Both Heart Failure With Preserved and Reduced Ejection Fraction**

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**(A)** Cigarette smoking was similarly associated with HF with preserved EF and HF with reduced EF, with adjusted HRs ~2 for current smoker (vs never). **(B)** Cigarette smoking cessation significantly reduced the risk of HFpEF and HFrEF, but excess HF risk persisted for a few decades. Results shown are from Cox model adjusting for age (years), race (Black, White), sex (male, female), education level, body mass index, total cholesterol, high-density lipoprotein cholesterol, drinking status (current, former, never), systolic blood pressure, blood pressure–lowering medication use, cholesterol-lowering medication use, kidney function, diabetes, and prevalent and incident coronary heart disease. All variables are time-varying variables. EF = ejection fraction; HF = heart failure; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LV = left ventricular; LVEF = left ventricular ejection fraction.

sex, race, and history of CHD. A longer duration of smoking cessation was associated with a lower risk for HF. Nonetheless, the excess risk persisted for up to a few decades after smoking cessation for both HFpEF and HFrEF (**Central Illustration**).

A few previous studies have evaluated the association of pack-years and smoking intensity with overall incident HF and reported significant dose-response relationships.[20-23] Our study comprehensively examined the impact of detailed smoking measures, including pack-years, intensity, and duration of smoking on HF, which confirmed and strengthened the evidence base. We also provide insights on the association of smoking measures with HFpEF and HFrEF, and found all smoking parameters consistently showed significant and similar associations with HFpEF and HFrEF.

It is not surprising that cigarette smoking was associated with increased risk of HFrEF because cigarette smoking is a significant risk factor for CHD, a major cause of HFrEF.[24,25] However, the etiological link between cigarette smoking and the development of HFpEF remains unclear. Nonetheless, there are several plausible mechanisms. For example, some studies showed the association of smoking with high blood pressure, a critical preceding condition of HFpEF.[26-28] Similarly, smoking increases arterial stiffness.[29,30] In addition, smoking induces oxidative stress and inflammation,[31] increasing left ventricular stiffness.[32] Moreover, tobacco smoke can cause cardiac mitochondrial dysfunction, a feature of HFpEF.[33,34] Further studies are needed to investigate underlying pathophysiological mechanisms linking smoking to HFpEF.

Previous studies have shown a reduction in the risk of overall HF with prolonged cessation. For example, the CHS (Cardiovascular Health Study) reported that former smokers who quit >15 years ago had a similar risk of HF as never smokers.[20] However, this previous study lumped all former smokers with over 15 years of cessation as 1 group. Our study uniquely examined the impact of smoking cessation by 10-year category over 3 decades on overall and 2 phenotypes of HF. We found a dose-response relationship for the duration of smoking cessation and risk of HF, and the residual risk persisted for a few decades for 2 phenotypes of HF.

Our study has important clinical and public health implications. First, experts have recommended lifestyle modifications for preventing HF, including weight loss, exercise, healthy diets, and sodium restriction.[35,36] Our results strengthened the evidence that smoking is an important modifiable risk factor for HF, and smoking cessation should be further emphasized in future public statements to prevent HF.[37] Second, HFpEF is increasingly recognized as a predominant form of HF worldwide.[38,39] Despite the increase in prevalence, evidence-based treatment for HFpEF is yet to be established. In this context, the strong association of smoking and HFpEF indicates the importance of smoking prevention in youth and young adults as well as early smoking cessation among cigarette smokers. Notably, a few therapeutic options have proven efficacy for smoking cessation.[40] Public health efforts and policymakers should emphasize the importance of smoking prevention and cessation to cope with the evolving public health issue of HFpEF.

**STUDY LIMITATIONS.** First, there might be potential measurement errors in the self-reported smoking status. Second, the baseline data was not available precisely at the beginning of 2005. There was, on average, a 6-month gap for variables based on annual phone interviews and a 7-year gap for variables collected at visit 4. However, we conducted analyses for overall HF using visit 1 as a baseline and found consistent results. Third, 15% of HF events could not be categorized into HF subtypes because of missing information on LVEF. Fourth, as in any observation study, residual confounding might exist (eg, household or local pollution and substance use). Fifth, we did not have information on cigars, pipes, or secondhand smoking around the baseline of the present study. Finally, the ARIC study did not collect information on e-cigarettes. It is unknown whether our findings apply to novel tobacco products like e-cigarettes. Given the increased prevalence of e-cigarette use, future studies are warranted to explore this topic.

## CONCLUSIONS

Cigarette smoking was significantly and similarly associated with HFpEF and HFrEF in a graded fashion. Smoking cessation significantly reduced the risk of HF, but its excess risk persisted for a few decades after cessation. Our results highlight the importance of smoking prevention and cessation for the prevention of HF, including HFpEF.

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## PERSPECTIVES

**COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS:** Cigarette smoking is associated with both HFpEF and HFrEF in a graded fashion. People smoking ≥25 pack-years have ~2-fold increased risk for HF compared with those who never smoked. Smoking cessation reduces the risk of HF, but excess risk persists for a few decades.

**TRANSLATIONAL OUTLOOK:** Public health policies and programs should emphasize avoidance and cessation of cigarette smoking to stem the high incidence of HF, including HFpEF.

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**KEY WORDS** **cigarette smoking, heart failure with preserved ejection fraction, heart failure with reduced ejection fraction, smoking cessation**


**APPENDIX** **For supplemental figures and tables, please see the online version of this paper.**