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Effect of an Intensive Lifestyle Intervention on Atrial Fibrillation Risk in Individuals with Type 2 Diabetes: the Look AHEAD Randomized Trial

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Abstract

Background—Obesity is associated with higher risk of atrial fibrillation (AF), but the impact of behavioral weight loss interventions on atrial fibrillation (AF) risk in persons with diabetes is unknown. We addressed this question in the Look AHEAD randomized trial.

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DISCLOSURES

None

Methods and Results—5067 overweight or obese individuals 45-76 years old with type 2 diabetes without prevalent AF were randomized to either an intensive lifestyle intervention (ILI) designed to achieve and maintain weight loss through caloric reduction and increased physical activity or to a diabetes support and education (DSE) usual care group. AF was ascertained from electrocardiograms at study exams and hospitalization discharge summaries. Multivariable Cox models were used to estimate the intention to treat effect of the intervention adjusting for baseline covariates. During a mean follow-up of 9.0 years, 294 incident AF cases were identified. Rates of AF were comparable in the ILI and DSE groups (6.1 and 6.7 cases per 1,000 person-years, respectively, p=0.42). The intervention did not affect AF incidence (multivariable hazard ratio [HR] 0.99, 95% confidence interval [CI] 0.77, 1.28). Similarly, neither weight loss nor improvement in physical fitness during the first year of the intervention were significantly associated with AF incidence: multivariable HR (95%CI) comparing top versus bottom quartile were 0.70 (0.41, 1.18) for weight loss and 0.88 (0.55, 1.43) for physical fitness improvement.

Conclusion—In a large randomized trial of overweight and obese individuals with type 2 diabetes, an ILI that induced modest weight loss did not reduce the risk of developing AF.

Keywords

atrial fibrillation; prevention; weight loss; type 2 diabetes; randomized trial

INTRODUCTION

Atrial fibrillation (AF) is a common arrhythmia in the general population, with an estimated lifetime risk of 25% and affecting >33 million individuals worldwide.[1, 2] AF increases the risk of stroke, heart failure, coronary heart disease, and total mortality, and is associated with added healthcare costs.[3, 4]

The etiology of AF is likely to be multifactorial, with hypertension and intrinsic cardiac causes, such as valvular disease and heart failure identified as independent risk factors. Obesity is also a well-established risk factor for AF.[5] In the Atherosclerosis Risk in Communities (ARIC) study, a large community-based cohort, presence of borderline or elevated cardiovascular risk factors explained >55% of the AF cases in the cohort, with overweight and obesity accounting for 18% of AF incidence.[6] Several other studies have found overweight and obesity to be strong determinants of AF risk.[7-10] Diabetes has also long been recognized as a risk factor for AF, increasing the risk of new-onset AF by 40%.[11] Physical activity and cardiorespiratory fitness, in contrast, show a more complex association with the risk of AF. Epidemiologic studies have shown that extreme levels of physical activity in endurance athletes increase AF incidence,[12] but recent reports suggest that higher levels of cardiorespiratory fitness in the range observed in the general population may be associated with lower AF risk.[13, 14]

As type 2 diabetes and AF share many common antecedents, including hypertension, atherosclerosis, and obesity, it is plausible that weight reduction may reduce the risk of developing new-onset AF. Indeed, a structured weight management program has been shown to significantly reduce symptom burden and severity in highly symptomatic individuals with AF, as compared to an intervention that attempted to optimize risk factors alone.[15] Similarly, long-term sustained weight loss in AF patients has been associated with reduction of arrhythmia burden and maintenance of sinus rhythm.[16] To our knowledge, no previous randomized studies, including trials of bariatric surgery or lifestyle-based weight-loss intervention, have determined whether a sustained weight loss intervention reduces the risk of new-onset AF in persons with type 2 diabetes.

Look AHEAD (Action for Health in Diabetes) was a multicenter, randomized clinical trial of an intensive lifestyle intervention (ILI) designed to achieve weight loss through caloric restriction and physical activity compared with a diabetes support and education (DSE) group in overweight and obese adults with type 2 diabetes. In the Look AHEAD trial, the ILI did not reduce the incidence of the primary endpoint of cardiovascular morbidity and mortality.[17] AF, however, was not part of the primary outcome. In the present secondary analysis of the Look AHEAD trial, we examined the impact of the ILI on the risk of newly-diagnosed AF. We hypothesized that individuals randomized to ILI, versus DSE, would have a lower risk of AF. In addition, we hypothesized that greater weight loss and improvement in physical fitness would be associated with lower AF incidence.

METHODS

Participants, Study Design, and Interventions

Look AHEAD randomly assigned 5,145 overweight or obese individuals with type 2 diabetes to ILI or DSE at 16 clinical sites across the United States. The study methods and baseline characteristics are described elsewhere,[18, 19] and the protocol is available at https://www.lookaheadtrial.org/public/LookAHEADProtocol.pdf. Participating centers received local IRB approval. Written informed consent was obtained from all participants.

Individuals were eligible if they were 45 to 76 years old, overweight or obese (body mass index, [BMI] ≥25 kg/m^2, or BMI ≥27 kg/m^2 in those taking insulin), able to complete a maximal exercise test to safely exercise, with treated or untreated systolic/diastolic blood pressure <160/100 mmHg, glycated hemoglobin (HbA1c) ≤11%, and had a primary health care provider. Exclusion criteria included inability to walk two blocks, non-traumatic amputation of a lower limb, urine dipstick protein of 4+ (equivalent to approximately >1 g protein/day), serum creatinine exceeding 1.4 mg/dl in women or 1.5 mg/dl in men, or current treatment with dialysis. There were no exclusions based on other complications of diabetes. Glucose-lowering medicines of any type were allowed and the use of insulin was limited to <30% of the cohort. Participants with and without a history of cardiovascular disease (CVD) were included. Additional inclusion and exclusion criteria have been published elsewhere.[19] For the present analysis, we also excluded participants with prevalent AF or atrial flutter at baseline (self-reported or present in the baseline study ECG).

At baseline, participants were randomized 1:1 to ILI or DSE. Initial treatment allocation was concealed to clinic staff; the assignment was revealed only after the participant was enrolled in the clinical trial. Outcomes assessors and laboratory staff were masked to treatment, but participants and interventionists were not because the intervention was behavioral. Those performing the statistical analyses for this report were not masked.

A detailed description of the interventions has been previously published.[20] In brief, the ILI aimed to achieve and maintain weight loss of at least 7% through reduced caloric intake and increased physical activity. The program included both group and individual counseling sessions, occurring weekly during the first 6 months, with decreasing frequency over the course of the trial. Strategies included a calorie intake goal of 1200 to 1800 kcal per day (with <30% of calories from fat and >15% from protein), meal-replacement products, and a physical activity goal of at least 175 minutes of moderate-intensity activity per week. Participants assigned to the DSE group received 3 group sessions per year that focused on diabetes education, diet, exercise, and social support for years 1 through 4 of the trial. In subsequent years, the frequency was reduced to 1 session annually. Participant's diabetes and cardiovascular risk factors were managed by their health care providers outside of Look AHEAD, with the exception of temporary changes in glucose-lowering medications that were made by study staff according to a specific algorithm to reduce the risk of hypoglycemia in the ILI group during periods of weight loss. Results of risk factor assessment at annual Look AHEAD data collection visits were provided to primary care physicians along with reminders of American Diabetes Association recommended targets for risk factor management. At the end of the study, mean weight loss from baseline was 6.0% in the ILI group and 3.5% in the DSE group; similarly, at year 4, physical fitness improved 3.7% in the ILI group and decreased 2.0% in the DSE group.[17]

On September 14, 2012, the intervention was terminated on the basis of a futility analysis and the subsequent recommendation from the Data and Safety Monitoring Board.[17] For the present analysis, we included AF cases identified through that date.

Covariate Assessment

At baseline and at subsequent annual visits, height and weight were measured in duplicate using a digital scale and stadiometer. Cardiorespiratory fitness was assessed at baseline, and years 1 and 4 using a graded exercise test. Details of the exercise tests and assessment of cardiorespiratory fitness in the Look AHEAD trial have been published elsewhere.[21] Briefly, a maximal graded exercise test was administered at baseline and a submaximal test at years 1 and 4. In both the maximal and submaximal exercise tests, cardiorespiratory fitness was defined similarly as the estimated metabolic equivalent (MET) level based on the treadmill workload (speed and grade) in which 80% of the maximal heart rate was attained among participants not taking β-blockers or a rating of 16 was reached on the rating of perceived exertion scale. Baseline-year 1 changes in fitness were computed as the percent difference between MET levels estimated using the approach described above.

Age, sex, race, smoking status, education, family income, and prior history of coronary heart disease and heart failure were self-reported at baseline. HbA1c was assessed from a fasting blood sample using standard methods at a central laboratory. Blood pressure was measured in duplicate using an automated device following a standardized protocol, and the average of the two measurements was used. Participants were asked to bring all their prescription medications to their assessments.

Study Outcome

Diagnosis of AF was obtained from 2 different sources: study electrocardiograms (ECGs) and hospitalization discharge diagnosis. Information on outpatient diagnosis of AF was not available. Participants underwent standard 12-lead ECG performed by a trained technician, masked to the intervention, at baseline and subsequently every 2 years. ECGs were electronically sent to the Look AHEAD ECG reading center at EPICARE (Wake Forest School of Medicine, Winston-Salem, NC) and were processed with the GE Marquette 12-SL program (GE Marquette, Inc., Milwaukee, WI). ECGs automatically coded as AF or atrial flutter were visually inspected by a trained cardiologist to confirm the diagnosis. Only visually confirmed new cases of AF or atrial flutter were considered to be events.

Information on AF occurrence was additionally collected from hospitalization discharge summaries. During annual study visits and telephone calls every 6 months, staff interviewers unaware of study-group assignment asked participants about medical events and hospitalizations. All relevant medical records were retrieved for adjudication of the trial primary and secondary endpoints. AF was considered present if the ICD-9-CM codes 427.31 or 427.32 were listed in any hospitalization not in the context of open cardiac surgery.

Incident time to AF was the study exam date in which the arrhythmia was diagnosed or the first hospitalization with a relevant ICD-9-CM discharge code, whichever occurred earlier.

Statistical Analyses

We estimated the effect of the ILI (vs the DSE intervention) on AF incidence using multivariable Cox proportional hazards regression, with time to AF as the main outcome variable. Time of follow-up was defined as the time in days from baseline to the earliest of AF incidence, death, lost to follow-up, last outcomes ascertainment or September 14, 2012, whichever was earlier. An initial model only adjusted for clinical site. A second model adjusted for clinical site, age, sex, and race. A third model adjusted additionally for education, family income, smoking, BMI, height, systolic and diastolic blood pressure, use of antihypertensive medications, HbA1c, prevalent coronary heart disease, and prevalent heart failure (all variables assessed at baseline). We tested the proportional hazards assumption including interaction terms between intervention status and time. No violations were observed. To assess the impact of method of case ascertainment on the estimates of association, we conducted additional analyses using AF events identified through each source (study ECG, hospital discharge codes) in separate models. We explored whether baseline BMI (dichotomized at 31.5 kg/m^2, the median value) or prevalent cardiovascular disease modified the effect of the ILI intervention including multiplicative terms between the effect modifier and the intervention group in the model and also performing a stratified analysis.

To assess the association of weight loss and improved fitness during the first year with the incidence of AF, we fit similar Cox models starting follow-up at the time of the year 1 visit, excluding individuals with AF occurring before that visit. Weight loss and improved fitness were categorized in quintiles, with the lowest quintile used as reference in multivariable models. P-values for trend were calculated modeling the quintile as a continuous variable.

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Additional models included weight loss and improved fitness as continuous variables. Finally, since previous observational studies have reported an interaction between physical activity and adiposity,[10, 22] we assessed the joint association of change in weight and physical fitness by categorizing participants into nine categories based on separate tertiles of weight change and physical fitness change, with those in the bottom tertile of both variables as the reference group.

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The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents.

RESULTS

Of the 5145 participants randomized, 61 were excluded due to presence of prevalent AF at baseline and an additional 17 were excluded because AF was reported solely on the basis of a severe adverse event during the follow-up. Table 1 shows baseline characteristics among 5067 eligible participants by intervention assignment. During a mean (median) follow-up of 9.0 (9.6) years, 294 cases of new-onset AF were identified. Of these 294 cases, 272 were identified from discharge hospitalizations and 97 from study ECGs (75 cases were identified through both sources) (Supplementary Table S1). The associations of selected baseline characteristics with risk of AF in this sample of overweight individuals with type 2 diabetes were similar to those observed in other populations (Table 2). Older age, higher BMI and height, use of antihypertensive medications, higher levels of HbA1c, and prevalent coronary heart disease were associated with significantly higher rates of AF.

Incidence of AF was comparable in both intervention arms (6.1 per 1,000 person-years in ILI and 6.7 per 1,000 person-years in DSE, p=0.42 for the comparison of the two rates). In fully-adjusted multivariable models, ILI did not affect the risk of developing newly-diagnosed AF compared to DSE (hazard ratio [HR] 0.99, 95% confidence interval [CI] 0.77-1.28) (Table 3 and Figure 1). A similar lack of effect was observed in additional analyses considering AF cases ascertained through each independent source, that is, study ECGs and hospital discharges (Supplementary Table S2). The effect of the ILI intervention did not differ by levels of baseline BMI (Supplementary Table S3), baseline physical fitness (Supplementary Table S4), or by prevalent CVD at baseline (Supplementary Table S5), p>0.05 for interaction in all analyses.

We examined whether weight loss and improved fitness during the first year after randomization was associated with the risk of AF. Compared to participants in the bottom quintile of weight loss, those in the top quintile did not have a significantly lower risk of AF (HR 0.70, 95%CI 0.41-1.18), after adjustment for multiple potential confounders (Table 4). Results were essentially unchanged when we used absolute weight loss rather than percent weight loss (data not shown). Similar lack of significant associations was observed for improved fitness (HR 0.88, 95%CI 0.55-1.43, comparing top versus bottom quintile; Table 5). We also explored the joint association of change in weight and physical fitness with the risk of AF categorizing individuals by tertiles of both variables. Risk of AF was not significantly different in any of these categories compared to individuals in the lowest tertiles of change in weight and physical fitness (Supplementary Table S6). Change in weight and change in physical fitness, modeled as continuous variables, did not interact in their association with AF (p for interaction = 0.80).

DISCUSSION

In this secondary analysis of the Look AHEAD randomized trial, an ILI designed to induce weight loss in people with type 2 diabetes did not reduce the risk of newly-diagnosed AF compared to a control intervention. These findings are consistent with the results for the Look AHEAD primary endpoint, in which the ILI did not reduce the risk of a composite endpoint of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, and hospitalized angina (HR 0.95, 95%CI 0.82, 1.09).[17] The lack of effect was consistent across subgroups of baseline BMI or prevalent CVD. Similarly, we did not find a significant association between weight loss or improved fitness during the first year of the intervention and the incidence of AF thereafter.

Numerous prospective cohorts have identified an increased risk of AF in overweight and obese individuals, compared to those with normal weight.[5-10, 23] Moreover, weight gain has also been found to be linked with increased AF risk. In the ARIC study, men who gained >10% of baseline weight over a 9 year period experience a 61% higher rate of AF compared to those gaining <5% (no association was found for weight gain and AF in women).[10] Similarly, in the Women's Health Study, risk of AF in women who became obese during a 5 year period was 41% higher during subsequent follow-up than among those who maintained BMI <30 kg/m^2.[9] Additional evidence has shown that higher levels of physical activity could ameliorate the adverse association between increased body mass and AF risk, with obesity being a weaker risk for AF among those physically more active.[10, 22, 24] Given the association between overweight/obese status and an increased risk of AF, we expected to observe a lower risk of AF with weight reduction. However, we failed to see a difference in the risk of AF between the ILI and DSE interventions, despite the fact that the ILI resulted in modest reduction in body weight. Additionally, we did not observe a statistically significant lower risk of AF in the subgroup of participants who lost the most weight or experienced the greatest improvement in physical fitness. To our knowledge, this analysis is the first to report the effect of a weight loss-focused lifestyle intervention in the risk of newly-diagnosed AF.

The lack of effect of weight loss and lifestyle modification in the Look AHEAD trial seems to be at odds with results from randomized and observational studies exploring the association of weight reduction lifestyle interventions in individuals with existing AF.[15, 16] In a randomized trial including 150 AF patients, Abed and colleagues showed that participants assigned to a weight loss intervention, compared to those in the control group (general lifestyle advice), experienced significant reductions in symptom burden scores, symptom severity scores, number of AF episodes, cumulative duration of AF, as well as reductions in interventricular septal thickness and left atrial area.[15] Similarly, the observational LEGACY Study reported that a sustained weight loss >10% was associated with lower arrhythmia burden and maintenance of sinus rhythm.[16] However, the participants in these studies were different from those in the Look AHEAD trial (patients with AF versus AF-free individuals with diabetes) and the degree of weight loss with the intervention was considerably higher in the LEGACY and Abed studies (>10%) compared to the Look AHEAD trial (6% at the end of the trial).

In light of the previous evidence, why was the ILI intervention in the Look AHEAD trial ineffective in reducing the risk of AF? Several reasons can be offered. First, the modest weight loss achieved in the intervention group and the minimal difference between groups may have not been enough to reduce the risk of AF. Second, as shown in the manuscript reporting the primary Look AHEAD results, use of cardioprotective drugs was lower in the ILI group compared to the DSE group, which could have contributed to the null results.[17, 25] Third, epidemiologic studies have found that very high levels of physical activity, such as that found in endurance athletes, are associated with increased risk of AF.[12] Higher risk of AF associated with increased physical activity in Look AHEAD participants may have masked a potential protective effect of weight loss. This mechanism, however, is unlikely given that the achieved levels of physical activity, generally brisk walking, are not comparable to those from studies in athletes, and also considering the lack of association of changes in physical fitness with AF risk in the Look AHEAD trial. Fourth, the lifestyle modification in the Look AHEAD trial included recommendations to consume 30% or fewer calories from fat.[18] Though there is no direct evidence to suggest that following this particular dietary advice could increase AF risk, other dietary patterns, such as the Mediterranean diet, have demonstrated efficacy in the primary prevention of AF compared to low-fat diets.[26] Fifth, all participants in Look AHEAD had type 2 diabetes. Therefore, our results do not rule out that a similar weight loss intervention could be effective in persons without diabetes. Sixth, we could not separate weight loss due to the intervention from that due to underlying comorbidities that may increase AF risk. Seventh, a potential effect of weight loss on the risk of AF may occur in a longer timeframe than that provided by the Look AHEAD trial, requiring extended follow-up. Finally, due to the limited number of events, our results cannot exclude a small effect of the intervention on AF risk.

The existing epidemiologic evidence suggests a complex interplay between physical activity, cardiorespiratory fitness, and the risk of AF. Very high levels of physical activity may be associated with increased risk of AF, particularly among younger individuals,[12, 27] while other studies have shown that moderate levels of physical activity could be protective.[10, 28] Our results, even though not showing a protective effect of increased cardiorespiratory fitness, suggest that moderate increases in physical activity levels are not associated with increased risk of AF. These findings should reassure clinicians and patients that initiating an exercise program, even in a high-risk population as people with type 2 diabetes, will not likely increase their risk of developing AF.

Incidence rates of AF in Look AHEAD (6.1-6.7 per 1000 person-years) were lower than AF rates observed in persons with diagnosed diabetes in the ARIC cohort (14.8 per 1000 person-years).[29] Differences in AF ascertainment, in the age and race composition, in the proportion of patients with diabetes using insulin (<30% by design in Look AHEAD), and in the distribution of cardiovascular risk factors between the two studies make this comparison problematic. However, in agreement with results from observational studies in community-based cohorts,[30] we identified age, white race, higher BMI and height, use of antihypertensive medication, and prevalent coronary heart disease as risk factors for the incidence of AF in the Look AHEAD trial. Higher levels of HbA1c at baseline were also associated with increased AF incidence, similar to findings in other populations.[29, 31]

Strengths and limitations

The current analysis has major strengths, such as being performed in the context of a large, well-conducted randomized trial with long follow-up. The study intervention led to clinically significant and sustained changes in weight and fitness and the ascertainment of AF cases was based on two independent sources.

While Look AHEAD had many strengths, there are limitations. AF was not a primary trial endpoint, and the specific analyses of AF were not pre-specified at the beginning of the trial. In addition, our method of AF ascertainment is certain to miss some individuals with paroxysmal or asymptomatic AF. Nonetheless, previous studies suggest that AF ascertainment using hospital discharge codes, one of the sources for case identification in the Look AHEAD trial, has adequate sensitivity and positive predictive value,[32, 33] and results were similar across different definitions of incident AF. Also, the number of events was probably insufficient to detect small effects: the estimated 95% confidence intervals are consistent with effects ranging from a 23% AF risk reduction to a 28% AF risk increase. The current results are from a secondary analysis of a completed trial, and future studies specifically designed to test the effect of lifestyle interventions on AF risk should be performed. Lastly, the results from the Look AHEAD trial may not generalize to individuals who do not have type 2 diabetes.

Conclusion

To conclude, among overweight and obese individuals with type 2 diabetes, an ILI that induced a modest weight loss did not reduce the risk of AF compared to diabetes support and education. Future studies should explore the inconsistencies between our results and those from previous interventional and observational studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Role of the Funding Source

The primary sponsor, the NIDDK, was represented on the Steering Committee and played a part in design and management of the Look AHEAD trial. The statistician (S.G.) had access to the raw data. Alvaro Alonso had full access to all results. All authors shared the final responsibility to submit for publication.

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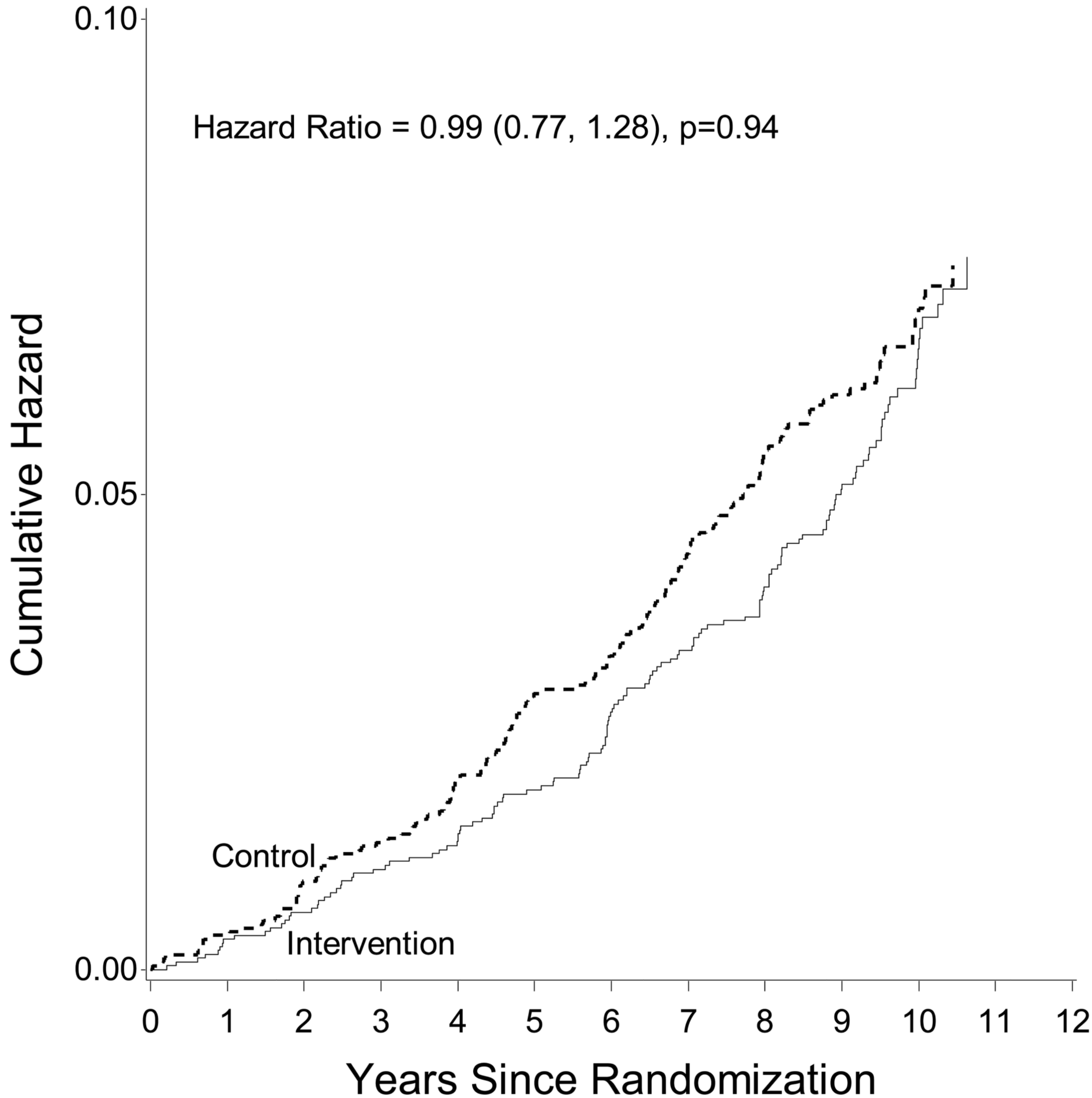

Figure 1.
Cumulative hazard of atrial fibrillation by intervention group, Look AHEAD, 2001-2012

Table 1

Baseline characteristics of study participants by intervention group, Look AHEAD, 2001-2004

	% or Mean (SD)	
	DSE	**ILI**
N	2539	2528
Age, years	59 (7)	59 (7)
Women	60%	60%
Race		
White	63%	63%
Black	16%	16%
Hispanic	13%	13%
Other	8%	8%
Completed high school	93%	93%
Family Income		
< $20K	12%	13%
$20K-$40K	21%	21%
$40K-$60K	20%	21%
$60K-$80K	16%	16%
> $80K	30%	29%
Current smoking	4%	5%
Baseline maximum METS	7.2 (2.0)	7.2 (2.0)
Body mass index, kg/m^2	36.0 (5.8)	35.9 (6.0)
Height, m	1.67 (0.10)	1.67 (0.10)
Systolic Blood pressure, mmHg	129 (17)	128 (17)
Diastolic Blood pressure, mmHg	70 (10)	70 (10)
Use of antihypertensive medication	72%	73%
Use of statins	45%	45%
HbA1c, %	7.3 (1.2)	7.2 (1.1)
Prevalent CHD	11%	11%
Prevalent heart failure	1%	1%

Table 2

Association of selected baseline characteristics with risk of AF, Look AHEAD, 2001-2012

Variable	HR (95% CI)
Age, per 5 years	1.45 (1.29, 1.64)
Sex (male vs female)	1.19 (0.77, 1.84)
Race/ethnicity	
White	1 (ref.)
Black	0.60 (0.39, 0.93)
Hispanic	0.65 (0.30, 1.39)
Other	1.10 (0.54, 2.25)
Body mass index, per 5 kg/m^2	1.23 (1.08, 1.39)
Baseline physical fitness, per 1 MET	0.90 (0.82, 0.99)
Height, per 10 cm	1.59 (1.28, 1.96)
Systolic blood pressure, per 15 mmHg	1.05 (0.92, 1.20)
Diastolic blood pressure, per 10 mmHg	0.96 (0.80, 1.15)
Use of antihypertensive medication	1.49 (1.04, 2.15)
Hb1Ac, per 1% increase	1.14 (1.02, 1.27)
Prevalent CHD	1.75 (1.27, 2.39)
Prevalent heart failure	2.05 (0.82, 5.10)

Multivariable Cox model simultaneously adjusted for variables in the table, education, income, intervention group, smoking status, and study site.

CHD: Coronary heart disease; CI: Confidence interval; HbA1c: Glycated hemoglobin; HR: Hazard ratio

Table 3

Effect of intervention on risk of AF, Look AHEAD, 2001-2012

	DSE	**ILI**	
AF events, n	153	141	
Person-years	22,691	22,957	
Incidence rate, per 1000 person-year	6.7	6.1	
	HR (95% Confidence interval)		P-value
Model 1	1 (ref.)	0.91 (0.72, 1.14)	0.42
Model 2	1 (ref.)	0.92 (0.73, 1.16)	0.47
Model 3	1 (ref.)	0.99 (0.77, 1.28)	0.94

DSE: Diabetes and Support Education group; HR: Hazard ratio; ILI: Intensive lifestyle intervention Model 1: Adjusted for clinic. Model 2: Adjusted for clinic, age, sex, and race. Model 3: Adjusted for clinic, age, sex, race, education, family income, smoking, body mass index, height, systolic blood pressure, diastolic blood pressure, use of antihypertensive medication, glycated hemoglobin, prevalent coronary heart disease, and prevalent heart failure.

Table 4

Association of weight change during first year of follow-up with subsequent risk of AF, Look AHEAD, 2001-2012

	Quintiles of weight change in first year of follow-up						
	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**P-value***	
Range (% weight loss)	29.2,0.9	0.9,−2.0	−2.0,−5.2	−5.2,−10.2	−10.2,−43.4		
AF events, n	54	53	60	46	51		
Person-years	8750	8920	8796	8815	8874		
Incidence, per 1000 py	6.2	5.9	6.8	5.2	5.8		
	Hazard ratio (95% confidence interval)						1-SD**
Model 1	1 (ref.)	0.95 (0.65, 1.38)	1.11 (0.77, 1.61)	0.84 (0.57, 1.24)	0.91 (0.62, 1.33)	0.48	0.98 (0.87, 1.11)
Model 2	1 (ref.)	0.88 (0.60, 1.29)	1.07 (0.74, 1.55)	0.80 (0.54, 1.19)	0.78 (0.53, 1.14)	0.18	0.95 (0.83, 1.06)
Model 3	1 (ref.)	0.90 (0.59, 1.38)	1.09 (0.71, 1.67)	0.79 (0.48, 1.30)	0.70 (0.41, 1.18)	0.20	0.93 (0.78, 1.10)

Model 1: Adjusted for clinic. Model 2: Adjusted for clinic, age, sex, and race. Model 3: Adjusted for clinic, age, sex, race, intervention group, education, family income, smoking, body mass index, height, systolic blood pressure, diastolic blood pressure, use of antihypertensive medication, glycated hemoglobin, prevalent CHD, and prevalent HF.

* P-value obtained from including quintile of weight loss as a continuous variable in the Cox model.

** 1-SD: Hazard ratio and 95% CI of AF per 1-standard deviation (7% weight loss) change in weight.

Table 5

Association of fitness change during first year of follow-up with incidence of atrial fibrillation, hazard ratios (95% confidence intervals), Look AHEAD, 2001-2012

	Improved fitness in first year of follow-up						
	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**P-value***	
Range (% improved fitness)	−52.9, −6.9	−6.8, 0	0.1, 13.5	13.6, 31.7	31.8, 185.7		
AF events, n	53	54	41	47	41		
Person-years	7948	8613	7300	8118	7982		
Incidence, per 1000 py	6.3	6.3	5.6	5.8	5.1		
	Hazard ratio (95% confidence interval)						1-SD**
Crude	1 (ref.)	0.91 (0.62, 1.34)	0.83 (0.55, 1.26)	0.87 (0.58, 1.29)	0.76 (0.50, 1.15)	0.20	0.89 (0.78, 1.03)
Age, sex, race adjusted	1 (ref.)	0.88 (0.60, 1.30)	0.89 (0.59, 1.34)	0.89 (0.60, 1.33)	0.80 (0.53, 1.22)	0.37	0.92 (0.80, 1.05)
Multivariable adjusted	1 (ref.)	0.82 (0.53, 1.26)	0.86 (0.55, 1.36)	0.89 (0.56, 1.39)	0.88 (0.55, 1.43)	0.76	0.98 (0.84, 1.16)

Model 1: Adjusted for clinic. Model 2: Adjusted for clinic, age, sex, and race. Model 3: Adjusted for clinic, age, sex, race, intervention group, education, family income, smoking, body mass index, height, systolic blood pressure, diastolic blood pressure, use of antihypertensive medication, glycated hemoglobin, prevalent coronary heart disease, and prevalent heart failure.

* P-value obtained from including quintile of fitness change as a continuous variable in the Cox model.

** 1-SD: Hazard ratio and 95% CI of AF per 1-standard deviation (27% improved fitness) change in improved fitness.