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Weight Loss in Older Patients With Persistent Atrial Fibrillation
The LOSE-AF Randomized Clinical Trial

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IMPORTANCE Excess body weight is a strong risk factor for atrial fibrillation (AF), and weight loss is recommended in clinical guidelines for all patients with obesity and AF. However, existing evidence derives from younger patients, and weight loss in older adults could precipitate frailty.

OBJECTIVE To investigate whether weight loss is a safe and effective intervention in older patients with overweight and AF.

DESIGN, SETTING, AND PARTICIPANTS Parallel-group, unblinded, randomized clinical trial conducted at 2 UK hospitals from November 14, 2018, to April 25, 2025. Approximately 1500 individuals undergoing electrical cardioversion for AF were assessed for eligibility, and approximately 500 aged 60 to 85 years with body mass index 27 or greater and without any exclusion criteria were invited to participate. Of these, 119 provided informed consent to enter the trial and 118 were randomized.

INTERVENTION Participants were randomized to an 8-month low-calorie diet and behavioral support program (intervention, n = 59) or to usual care (control, n = 59).

MAIN OUTCOME AND MEASURE Intention-to-treat analysis of the change in Atrial Fibrillation Severity Scale (AFSS) symptom severity score at 8 months after randomization.

RESULTS Participants (n = 118) had a mean age of 68 years (SD, 6); 33% were female. The intervention resulted in significantly lower weight (baseline-adjusted mean weight at 8 months: 92.6 [SE, 0.85] kg vs 99.4 [SE, 0.85] kg; *P* < .001; estimated difference, −6.9 kg [95% CI, −9.2 to −4.5]). This corresponded to a weight reduction of 9.7% vs 3.1%, respectively (*P* < .001). However, there were no significant differences between the groups in AFSS symptom severity score (baseline-adjusted mean at 8 months, 7.9 [SE, 0.84] in the intervention group vs 8.9 [SE, 0.84] in the control group; between-group difference, −0.9 [95% CI, −3.3 to 1.4]; *P* = .43). No significant treatment effects were observed on physical performance, AF burden, cardiac imaging parameters, blood pressure, lipid profile, or incidence of repeat cardioversion or AF ablation during follow-up. No serious adverse events related to participation in the trial were reported in either group.

CONCLUSIONS AND RELEVANCE In older patients with overweight and persistent AF, a low-calorie diet and behavioral support program was associated with significant weight loss at 8 months with no safety concerns but did not affect AF symptoms, AF burden, cardiac remodeling, or the need for further rhythm control interventions.

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Visual Abstract

Research Summary

Editorial

Supplemental content

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Atrial fibrillation (AF) affects more than 50 million individuals worldwide[1] and represents a burgeoning public health epidemic.[2,3] Prevalence rises sharply with advancing age,[4] and AF is frequently accompanied by physical frailty and reduced functional capacity in older adults.[5,6] Excess body weight has emerged as the strongest modifiable risk factor for incident AF, with increased body mass index (BMI) independently associated with AF onset, progression, and recurrence.[7-11]

Weight loss has a class I recommendation in clinical guidelines for patients with obesity and AF, targeting a loss of 10% or more of body weight.[12,13] Structured interventions based on low-energy diets (800-1200 kcal/d) can achieve meaningful weight loss, better glycemic control, and lower blood pressure in individuals with overweight or obesity.[14,15] However, existing randomized trials and observational studies of such interventions have included younger patients with AF (mean age, ≈60 years).[15-19] More typical older patients with AF are often characterized by longer disease duration, higher prevalence of comorbidities, and increased susceptibility to sarcopenia and frailty.[20-22] In this setting, intentional weight loss may yield a less favorable risk-benefit profile, potentially limiting its therapeutic value.[20-22]

The LOSE-AF trial investigated whether dietary weight loss could safely and effectively improve AF-related outcomes, including AF-related symptoms, AF burden, cardiac remodeling imaging parameters, and serum biomarker levels, in older patients with persistent AF referred for direct current cardioversion (DCCV).

Key Points

Question In older patients with overweight and atrial fibrillation (AF) undergoing cardioversion, does dietary weight loss improve AF-related symptoms compared with usual care?

Findings In this randomized clinical trial that included 118 individuals, the baseline-adjusted mean Atrial Fibrillation Severity Scale symptom severity score at 8 months was not significantly different between the groups (7.9 [SE, 0.84] in the intervention group vs 8.9 [SE, 0.84] in the control group, $P = .43$) despite the intervention resulting in significantly lower body weight (92.6 [SE, 0.85] kg vs 99.4 [SE, 0.85] kg; $P < .001$).

Meaning Moderate dietary weight loss was not an effective treatment strategy in this trial in older patients with persistent AF.

Methods

Study Design

LOSE-AF is a prospective, open-label, randomized clinical trial. Individuals aged 60 to 85 years with persistent AF, referred for DCCV, and with BMI of 27 or greater (calculated as weight in kilograms divided by square of height in meters) were recruited. Participants were randomized (1:1) to receive either an 8-month structured dietary weight loss and behavioral support program (intervention) or usual care, consisting of a one-off, nurse-led consultation and supporting written material (control).

Participants underwent a baseline visit prior to randomization and a follow-up visit approximately 8 months later. Both visits included assessment of AF symptoms using the Atrial Fibrillation Severity Scale (AFSS),[23] anthropometric measurements, clinical history, 12-lead electrocardiogram (ECG), Physical Performance Testing (PPT) to evaluate functional capacity,[24] quality-of-life (QoL) assessment using the EuroQoL 5-Dimension 5-Level (EQ-5D-5L) health status measure, cardiovascular magnetic resonance (CMR) imaging, and blood sampling. At the 8-month follow-up, participants also underwent extended (14-day) ECG patch monitoring (BodyGuardian MINI, Boston Scientific). Additional interim assessments were conducted via mail or telephone at approximately 4 months and at the study end, including AFSS and QoL questionnaires. The study protocol is available in Supplement 1 and the statistical analysis plan in Supplement 2.

Participants

Participants were recruited from 2 UK hospitals (John Radcliffe Hospital, Oxford, and Milton Keynes University Hospital). Key exclusion criteria included planned catheter ablation for AF within 8 months; recent participation in a weight loss program or unintentional weight loss greater than 5 kg; current use of antiobesity medications; uncontrolled endocrine disorders; insulin-treated diabetes; significant medical or psychiatric comorbidities; stage 4/5 chronic kidney disease; and inability to provide informed consent (see eTable 1 in Supplement 3 for complete eligibility criteria).

All participants provided written informed consent. The study protocol was approved by a research ethics committee (18/EM/0197) and the University of Oxford. This study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines.

Randomization

Participants were randomized 1:1 to intervention (structured dietary weight loss and behavioral support program) or control (usual care) using a web-based system. A mixed-block design (with varying block sizes) stratified by sex[25] ensured allocation concealment prior to randomization. The randomization schedule was created by the trial statistician and was not accessible to other trial investigators or recruiting personnel.

There was no masking, and participants and investigators were aware of study group allocation. However, subjective end points such as imaging and ECG monitoring were analyzed by observers blinded to treatment allocation and clinical information.

Procedures

Intervention Group

Participants randomized to the intervention group were referred to a commercial provider of a structured dietary weight loss and behavioral support program. Each participant was assigned a local counselor who provided regular, individually tailored appointments over a 32-week period to deliver behavioral coaching, monitor weight, and supply formula meal products (see eMethods in Supplement 3 for full details).

Control Group

Participants allocated to the control group received usual care, consisting of a single face-to-face consultation with a research nurse and written materials on dietary weight loss.

Clinical Management

Decision-making regarding initial referral for DCCV, pharmacological therapy, and subsequent AF-related interventions (eg, repeat DCCV or catheter ablation) was at the discretion of the treating physician.

Physical Performance Test

Physical performance was assessed using the modified PPT, which evaluates the ability to perform activities of daily living. The test yields a maximum score of 36, with lower scores indicating poorer physical function. Reduced PPT scores are associated with increased frailty, impaired mobility, and higher mortality risk in older adults.[24,26] The composite score comprises performance across timed functional tasks (detailed in Supplement 3).[27,28]

Cardiac Magnetic Resonance and Spectroscopy

Cardiac magnetic resonance imaging and phosphorus-31 spectroscopy were performed on a 3.0 Tesla system (Magnetom Prisma; Siemens Healthineers). Further details are reported in the eMethods in Supplement 3.

Outcomes

The primary outcome was AF symptom severity at 8 months, assessed using the symptom severity subscale of the AFSS. The AFSS is a validated instrument that includes 2 subscales: one measuring symptom severity (ranging from 0 [no symptoms] to 35 [severe symptoms]) and another assessing symptom burden (ranging from 3.25 [single minimally symptomatic episode lasting minutes] to 30 [continuous and highly symptomatic episodes lasting more than 48 hours]).[23]

Key secondary outcomes (all assessed at 8 months) included AF burden, defined as the percentage of time spent in AF during 14-day continuous ECG monitoring; physical performance, evaluated using the PPT; and body weight, measured using calibrated electronic scales.

Additional secondary outcomes assessed at 8 months included QoL (measured using the EQ-5D-5L utility score); cardiac structure and function (evaluated by CMR imaging); blood pressure; and circulating biomarkers. Postrandomization events such as repeat DCCV and AF ablation were recorded to assess differences in downstream clinical management between the intervention and control groups.

Long-term follow-up data were collected by reviewing electronic patient records and by postal/telephone questionnaires.

Statistical Analysis

The trial was originally designed with a primary outcome of freedom from AF recurrence, with a sample size of 180 individuals. Because of the impact of the COVID-19 pandemic on the trial recruitment, the trial protocol was amended, and the primary outcome was changed to the detection of a clinically meaningful difference in AF symptom severity at 8 months, measured using the AFSS symptom severity score.[23] Pilot data indicated a mean baseline score of approximately 13, with a standard deviation of 6. A between-group difference of 4 points was considered clinically relevant.[29] Assuming an adherence rate of 85% in the intervention group,[14] a total sample size of at least 100 participants (50 per group) was estimated to provide 80% power to detect the target treatment effect at a 2-sided α level of .05.

All analyses adhered to the intention-to-treat principle, with participants analyzed in their originally assigned groups irrespective of treatment adherence or whether DCCV was ultimately performed. Missing data were summarized by treatment group.

The primary outcome (AFSS symptom severity score at 8 months) was analyzed using analysis of covariance with adjustment for baseline values. Similarly, analysis of covariance was used for the secondary outcomes (body weight, PPT score, and EQ-5D-5L visual analog scale score). Log transformation was applied when required to meet model assumptions. The *t* test was used to compare all other continuous secondary outcomes between groups.

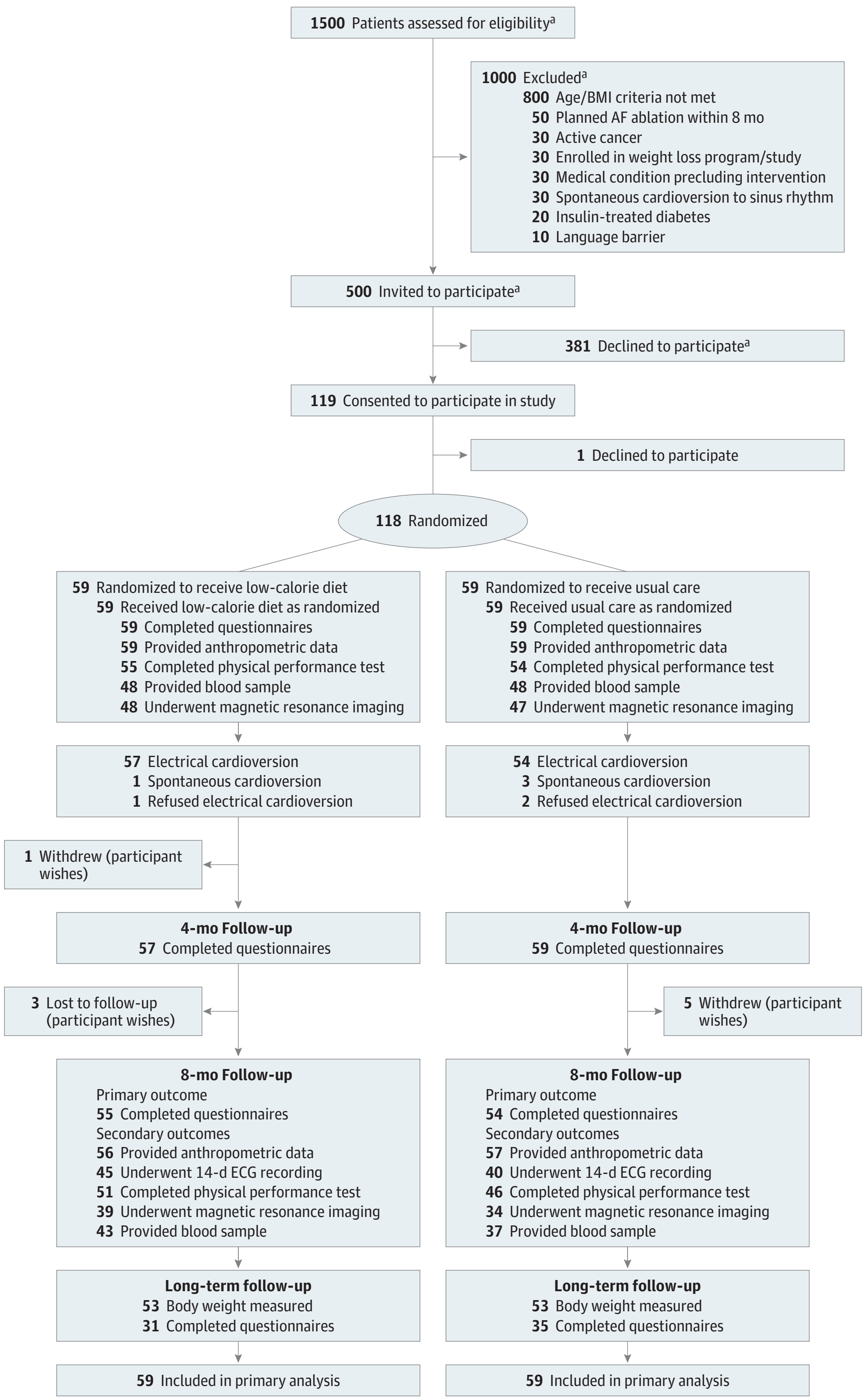
All statistical tests were 2-sided, with significance defined as $P < .05$. Analyses were performed using SPSS Statistics version 31.0 (IBM Corp). Detailed descriptions of the statistical analysis are provided in the eMethods in Supplement 3 and the statistical analysis plan (Supplement 2).

Results

Between November 2018 and July 2024, approximately 1500 individuals undergoing electrical cardioversion for AF were assessed for eligibility. Of these, approximately 500 aged 60 to 85 years with BMI of 27 or greater and without any exclusion criteria were invited to participate. One hundred nineteen participants were recruited and provided informed consent. One participant withdrew prior to randomization, resulting in a final cohort of 118 patients: 59 randomized to the intervention group and 59 to the control group (**Figure 1**).

Baseline demographic, anthropometric, and clinical characteristics are summarized in **Table 1**. All participants completed the baseline visit and the AFSS. The primary outcome (AFSS symptom severity score at 8 months) was completed by 109 participants (55 intervention, 54 control). Nine participants did not complete the primary outcome assessment: 3 (all in the intervention group) were lost to follow-up, and 6 (1 in the intervention group, 5 in the control group) withdrew consent, all citing a lack of interest in continuing. At the 8-month follow-up, anthropometric data were available in 113 participants (56 intervention, 57 control), and the EQ-5D-5L was completed by 109 participants (55 intervention, 54 control). Long-term follow-up data on body weight were available in 106 participants (53 per group) at a mean of 3.5 (SD, 1.8) years. Full details of the number of participants completing the other secondary and other outcome assessments are reported in Figure 1. No serious adverse events related to the trial intervention or study participation were reported in either group.

Figure 1. Flowchart of Recruitment, Randomization, and Analytic Groups in a Trial of Dietary Weight Loss to Improve Atrial Fibrillation–Related Symptoms



For participants who withdrew, were lost to follow-up, or missed measurement visits, missing 8-month values were replaced by the 4-month value when available, or by the baseline value if the 4-month measurement was unavailable, for the primary outcome, the secondary outcomes of body weight and Physical Performance Test score, and the other outcome of quality-of-life visual analog scale score. The secondary outcome of atrial fibrillation (AF) burden was dichotomized into zero AF burden vs nonzero AF burden. Participants were classified as having nonzero AF burden if AF was detected on 14-day electrocardiographic (ECG) monitoring or the 12-lead ECG at 8 months; otherwise, they were classified as having zero AF burden. Ten participants lacked 8-month ECG data and were assumed to have nonzero AF burden in the main analysis. For all other outcomes, analysis compared mean (SE) values at the 8-month visit, with any missing 8-month values replaced with the baseline value. BMI indicates body mass index.

[a] Approximate estimate.

Weight Loss, AF Symptoms, Quality of Life, Freedom From AF, and Physical Performance

The intervention produced substantially greater weight loss than usual care. Baseline-adjusted mean body weight was lower in the intervention group at both 4 months (93.4 [SE, 0.64] kg vs 98.1 [SE, 0.64] kg; $P < .001$; estimated difference, 4.7 kg [95% CI, 2.9-6.5]) and 8 months (92.6 [SE, 0.85] kg vs 99.4 [SE, 0.85] kg; $P < .001$; estimated difference, 6.9 kg

Table 1. Baseline Characteristics

Characteristic	Randomized allocation	
	Low-calorie diet (n = 59)	Control (n = 59)
Age, mean (SD), y	68.5 (5.5)	68.3 (5.7)
Sex, No. (%)		
Male	39 (66)	40 (68)
Female	20 (34)	19 (32)
Anthropometric data		
Weight, mean (SD), kg	103.2 (16.2)	101.9 (16.8)
Height, mean (SD), m	1.73 (0.1)	1.73 (0.1)
BMI, mean (SD)[a]	34.6 (4.8)	34.1 (5.4)
BMI category, No. (%)[a]		
>30	46 (78)	43 (73)
>35	21 (36)	25 (42)
>40	11 (9)	7 (12)
Body surface area, mean (SD), m^2	2.2 (0.2)	2.2 (0.2)
Vital signs		
Heart rate, mean (SD), beats/min	78 (17)	76 (15)
Systolic blood pressure, mm Hg		
Mean (SD)	135 (19)	132 (18)
>140, No./total (%)	18/55 (33)	15/53 (28)
Diastolic blood pressure, mm Hg		
Mean (SD)	81 (11)	80 (13)
>90, No./total (%)	13/55 (24)	14/53 (26)
CHA_2DS_2VASc score, median (IQR)	2 (2-3)	2 (1-3)
Comorbidities, No. (%)		
Hypertension	42 (71)	48 (81)
Diabetes	7 (12)	3 (5)
Heart failure	6 (10)	9 (15)
Stroke or TIA	6 (10)	3 (5)
Vascular disease	1 (2)	6 (10)
Peripheral vascular disease	1 (2)	0 (0)
Prior myocardial infarction	0 (0)	1 (2)
Alcohol use >8 U/wk, No. (%)	7 (12)	6 (10)
Medications, No./total (%)		
Oral anticoagulation	58/58 (100)	58/58 (100)
Direct oral anticoagulant	49/58 (84)	54/58 (93)
Vitamin K antagonist	9/58 (16)	4/58 (7)
β-Blocker	49/58 (84)	49/58 (84)
RAAS inhibition	29/58 (50)	30/58 (52)
Statin	29/58 (50)	30/58 (52)
Diuretic	20/58 (34)	15/58 (26)
Amiodarone	17/58 (29)	5/58 (9)
Calcium channel blocker	14/58 (24)	16/58 (28)
Antiplatelet	3/58 (5)	1/58 (2)
Sotalol	3/58 (5)	7/58 (12)
Ezetimibe	2/58 (3)	0/58 (0)
SGLT-2 inhibitor	3/58 (5)	2/58 (3)
Class I antiarrhythmic	1/58 (2)	1/58 (2)

(continued)

Table 1. Baseline Characteristics (continued)

Characteristic	Randomized allocation	
	Low-calorie diet (n = 59)	Control (n = 59)
AF characteristics		
Long-standing persistent AF, No. (%)	26 (44)	30 (51)
Previous DC cardioversion, No. (%)	28 (47)	16 (27)
Previous AF ablation, No. (%)	12 (20)	10 (17)
AF duration, median (IQR), mo	9.6 (4.2-54)	13.1 (5-49)
AFSS symptom severity score, mean (SD)[b]	13.8 (5.9)	12.8 (5.9)
AFSS symptoms burden score, mean (SD)	24.4 (3.7)	24.2 (4.0)
PPT score, mean (SD)[c]	31.9 (3.3) [n = 55]	31.9 (3.5) [n = 54]

Abbreviations: AF, atrial fibrillation; AFSS, Atrial Fibrillation Severity Scale; BMI, body mass index; CHA_2DS_2VASc, congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/transient ischemic attack/thromboembolism, vascular disease, age 65-74 years, sex; DC, direct current; PPT, Physical Performance Test; RAAS, renin-angiotensin-aldosterone system; SGLT-2, sodium-glucose cotransporter 2; TIA, transient ischemic attack.

[a] Calculated as weight in kilograms divided by square of height in meters.

[b] Score ranges from 0 to 35, with higher scores indicating more severe symptoms. A difference of 4 points was considered clinically relevant.[29]

[c] Score ranges from 0 to 36, with higher scores indicating better physical performance.

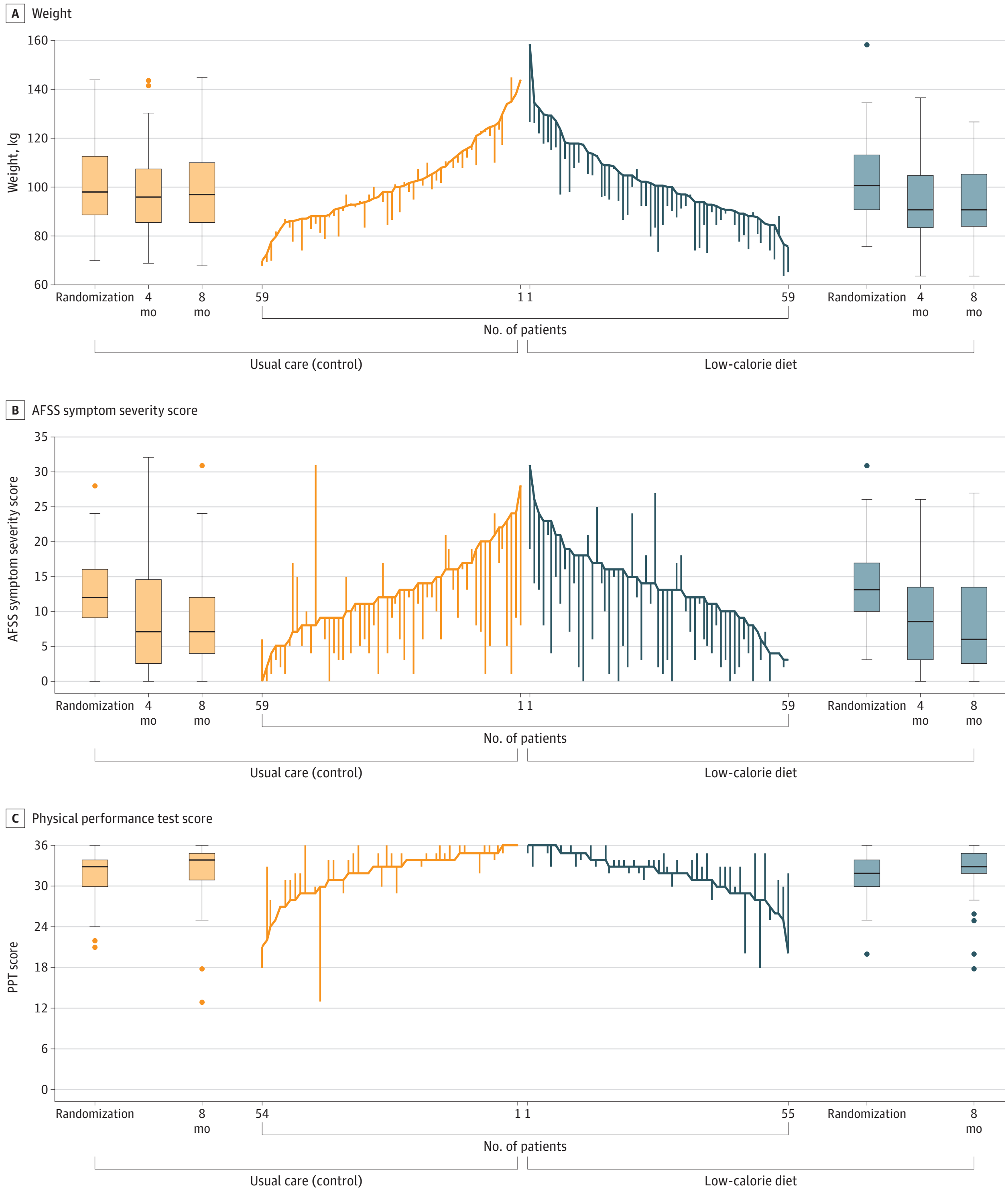
[95% CI, 4.5-9.2]) (**Figure 2**A). This corresponded to weight reduction from baseline to 8 months of 9.7% in the intervention group vs 3.1% in the control group (*P* < .001).

Despite these differences in weight, no significant between-group differences were observed in AFSS symptom severity scores at 4 months (8.8 [SE, 0.88] vs 9.3 [SE, 0.88]; *P* = .21) or 8 months (7.9 [SE, 0.84] vs 8.9 [SE, 0.84]; *P* = .43; between-group difference, −0.9 [95% CI, −3.3 to 1.4]) (Figure 2B). Prespecified subgroup analyses for the primary outcome showed no evidence of treatment effect modification by sex, age, or baseline BMI (all *P* > .05) (eFigure 2 in Supplement 3). AFSS symptom burden scores were also similar between groups at 4 months (15.5 [SE, 1.15] vs 16.2 [SE, 1.15]; *P* = .70) and 8 months (15.8 [SE, 1.08] vs 15.0 [SE, 1.08]; *P* = .59) (eFigure 1 in Supplement 3). Importantly, weight loss did not adversely affect functional status, with PPT scores at 8 months identical between the intervention and control groups (32.6 [SE, 0.44] vs 32.6 [SE, 0.44]; *P* = .99) (Figure 2C).

Health-related quality of life, assessed using the EQ-5D-5L visual analog scale, did not differ significantly between the intervention and control groups at 4 months (73.6 [SE, 2.07] vs 71.2 [SE, 2.07]; *P* = .41) or 8 months (75.3 [SE, 1.90] vs 74.2 [SE, 1.89]; *P* = .70).

Freedom from AF at follow-up was similar in the intervention and control groups (42% vs 49%; estimated difference, −6.8% [95% CI, −26.4 to 12.8]; *P* = .58), with median AF burden of 0% (IQR, 0%-100%) in both groups in participants who completed 14-day ECG monitoring (eFigure 3 in Supplement 3). Among patients with AF recorded during ECG monitoring, the median AF burden was 100% (IQR, 62.9%-100%) in the intervention group and 100% (IQR, 80%-100%) in the control group.

Figure 2. Parallel-Line Plot of Weight, Atrial Fibrillation Symptoms, and Physical Performance During the Intervention Period



Curves show the paired data for individuals at randomization and 8 months. Each line represents 1 participant; participants are ordered by their value at randomization, with highest randomization values positioned centrally. Box plots summarize the distribution of values at randomization, 4 months, and 8 months. Box elements represent the lower, median, and upper quartiles. The lower whiskers extend to the minimum value that is no more than 1.5x the IQR below the lower quartile, and the upper whiskers extend to the maximum value that is no more than 1.5x above the upper quartile. Outliers beyond these points are shown as dots. Missing data were replaced with the value at the previous visit (4 months or randomization). The Atrial Fibrillation Severity Scale (AFSS) score ranges from 0 to 35; a reduction in AFSS reflects improvement in symptoms, and a difference of 4 points was considered clinically relevant.[29] For the Physical Performance Test (PPT), 4 patients allocated to low-calorie diet and 5 patients to control did not have a value at randomization; these patients do not contribute to panel C. PPT scores range from 0 to 36; higher scores indicate better physical performance.

Medication use at follow-up is shown in eTable 2 in Supplement 3.

Cardiac Magnetic Resonance and Laboratory Data

At the follow-up CMR, 43% of participants were experiencing AF (44% in the intervention group vs 42% in the control group). There were no significant differences between the groups in any measured parameter of atrial or ventricular structure or function (**Table 2**). Likewise, there were no significant differences in blood pressure or in levels of total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, C-reactive protein, interleukin 6, or N-terminal pro–brain natriuretic peptide between the groups (Table 2).

Exploratory Long-Term Follow-Up

At long-term follow-up of 3.5 (SD, 1.8) years, those in the intervention group still had a significantly lower body weight than those in the control group (95.6 [SE, 1.00] kg vs 100.5 [SE, 1.00] kg; $P < .001$; estimated difference, 4.9 kg [95% CI, 2.1-7.7]). However, no significant differences were observed in long-term AFSS symptom severity, symptom burden, or EuroQoL visual analog scale scores (all $P > .05$) (eTable 3 in Supplement 3).

There were no significant between-group differences in AF recurrence following the index cardioversion (hazard ratio [HR], 1.04 [95% CI, 0.69-1.58]; $P = .85$) (eFigure 4A in Supplement 3), repeat DCCV (HR, 0.64 [95% CI, 0.35-1.16]; $P = .14$) (eFigure 4B in Supplement 3), or AF ablation (HR, 1.00 [95% CI, 0.48-2.10]; $P > .99$) (eFigure 4C in Supplement 3).

Discussion

In this randomized clinical trial in older patients with persistent AF undergoing DCCV, a structured low-calorie diet and behavioral support program led to a 9.7% reduction in body weight at 8 months, without any serious adverse events or functional decline related to the study intervention. However, the intervention did not affect AF symptoms, AF recurrence, AF burden, atrial structural remodeling, or the need for further rhythm control interventions.

Abed et al[16] reported that the combination of dietary weight reduction and intensive management of cardiometabolic risk significantly improved AF burden and symptom severity at 15 months in relatively young patients (mean age, 60 years) with paroxysmal or persistent AF and BMI of 27 or greater, who were all in sinus rhythm at the time of recruitment. The findings are limited by a high rate of withdrawal after randomization and loss to follow-up (together meaning that the primary results are based on only 46% [81/178] of individuals originally randomized), while the bespoke multidisciplinary approach used is not easily accessible to most clinicians. This is the only randomized trial supporting the current class I recommendation for weight loss in individuals with overweight and obesity and AF in international guidelines.[12,13]

The current study aimed to address the knowledge gap regarding the value of weight loss in typical older patients with AF. In addition to being older, almost half the participants in the current study had long-standing persistent AF, suggesting more advanced atrial remodeling than those in previous trials. These factors are all associated with treatment resistance and more complex arrhythmia mechanisms[30] and may indicate reduced capacity of the atrial myocardium for reverse structural or electrical remodeling.[31] Perhaps for this reason, the 9.7% weight loss in the intervention group was not associated with a reduction in AF-related symptoms, AF recurrence, or CMR imaging measures of cardiac remodeling at 8-month follow-up. There were also no significant differences in AF-related symptoms or quality of life between the groups at 3.5 years, despite persistently lower body weight in the intervention group.

The impact of weight reduction on AF-related symptoms was assessed using the AFSS score, consistent with previous randomized and observational studies. In prior studies, symptomatic improvement was generally observed alongside substantial reductions in AF burden, suggesting that meaningful symptom relief may depend on the restoration or maintenance of sinus rhythm. In the current study, there was no significant difference between the groups in AF burden at 8-month follow-up. Because the AFSS score is designed to predominantly capture changes in symptoms due to rhythm status, it may have limited sensitivity to detect any wider symptomatic benefit of weight reduction, unrelated to a change in AF burden.

The study had a pragmatic design, with the intervention consisting of referral to a relatively inexpensive and commercially available dietary weight loss and behavioral support program that could be deployed nationally, rather than relying on specialized clinics with limited geographic coverage. The strategy was highly effective, achieving a magnitude of intention-to-treat weight loss similar to that achieved in a trial using a bespoke clinic.[16] It is also notable that the 8-month intervention in the current study led to a persistent between-group weight difference at an average of 3.5 years after randomization. This degree and duration of weight loss would be expected to have holistic benefits beyond AF[32] but did not affect AF-related symptoms. Indeed, similar degrees of weight loss (−9.4%) achieved pharmacologically reduced major adverse cardiovascular events over a mean follow-up duration of 40 months in individuals with preexisting cardiovascular disease and elevated BMI.[33] Further research is needed to establish the potential impact of pharmacological approaches leading to weight loss in patients with overweight and AF.

The study results are consistent with those of other recent randomized trials investigating weight loss in patients with AF[17,18]; together, these data suggest that the effect of weight loss on AF outcomes may be more modest than the larger effect size seen in the original trial by Abed et al[16] and in prior observational studies[15,19] (eTable 4 in Supplement 3). These findings are also consistent with those from a recent meta-analysis that reported heterogeneous and overall modest effects of weight loss interventions on AF-related outcomes, largely driven by studies in younger populations with less advanced AF and intensive, multimodal risk-factor management strategies, with more evident benefits observed in

Table 2. Study Outcomes at 8 Months

Outcome	Mean (SE) Low-calorie diet (n = 59)	Mean (SE) Control (n = 59)	Absolute or percentage difference (95% CI)	*P* value
Primary outcome				
AFSS symptom severity score[a,b]	7.9 (0.84)	8.9 (0.84)	−0.9 (−3.3 to 1.4)	.43
Secondary outcomes				
Body weight, kg[a]	92.6 (0.85)	99.4 (0.85)	−6.9 (−9.2 to −4.5)	<.001
AF burden of zero, No. (%)	25 (42)	29 (49)	−6.8 (−26.4 to 12.8)	.58
PPT score[a,c]	32.6 (0.44)	32.6 (0.44)	0 (−1.2 to 1.2)	.99
Other outcomes				
Quality-of-life VAS[a,d]	75.3 (1.90)	74.2 (1.89)	1.1 (−4.3 to 6.4)	.70
AFSS symptom burden score[e]	15.8 (1.08)	15.0 (1.08)	0.8 (−2.2 to 3.8)	.59
Cardiac structure and function by cardiac MRI				
LA volume, mL	118.3 (5.17)	123.6 (5.34)	−5.3 (−20.1 to 9.4)	.48
Index LA volume, mL/m^2	55.8 (2.51)	57.3 (2.60)	−1.5 (−8.6 to 5.8)	.69
LA ejection fraction, %	33.5 (2.28)	30.6 (2.35)	2.9 (−3.6 to 9.4)	.38
LA reservoir strain, %	18.2 (1.62)	16.9 (1.65)	1.3 (−3.3 to 5.9)	.56
LVED volume, mL	156.7 (6.78)	157.1 (6.92)	−0.4 (−19.6 to 18.9)	.97
Index LVED volume, mL	73.2 (2.86)	72.4 (2.92)	0.8 (−7.4 to 8.9)	.85
LV ejection fraction, %	55.6 (1.62)	55.0 (1.66)	0.6 (−3.9 to 5.3)	.78
LV longitudinal strain, %	15.0 (0.60)	15.0 (0.62)	0.0 (−1.7 to 1.7)	.97
Myocardial mass, g	114.9 (4.18)	112.9 (4.27)	2.0 (−9.9 to 13.8)	.74
Index myocardial mass, g/m^2	53.7 (1.57)	52.0 (1.60)	1.7 (−2.8 to 6.1)	.45
RVED volume, mL	165.9 (6.54)	160.6 (6.75)	5.3 (−13.4 to 24.0)	.57
Index RVED volume, mL	77.3 (2.85)	74.6 (2.94)	2.7 (−5.5 to 10.8)	.52
RV ejection fraction, %	52.4 (1.43)	53.3 (1.48)	−0.9 (−5.0 to 3.2)	.65
Cardiac PCr/ATP ratio by ^{31}P MRS	1.66 (0.07)	1.52 (0.08)	0.14 (−0.06 to 0.35)	.16
Blood pressure, mm Hg				
Systolic	138.1 (2.69)	137.5 (2.60)	0.6 (−6.9 to 8.0)	.88
Diastolic	77.8 (1.00)	78.1 (1.49)	−0.3 (−4.3 to 3.7)	.88
Blood biomarkers[f]				
Total cholesterol, mmol/L	4.55 (0.16)	4.72 (0.16)	−0.17 (−0.62 to 0.28)	.46
LDL-C, mmol/L	2.28 (0.13)	2.56 (0.13)	−0.28 (−0.64 to 0.09)	.14
HDL-C, mmol/L	1.34 (0.04)	1.27 (0.04)	0.07 (−0.04 to 0.19)	.19
Triglycerides, mmol/L	1.31 (0.09)	1.41 (0.09)	−0.10 (−0.35 to 0.14)	.39
hsCRP, mg/dL	1.90 (0.31)	1.95 (0.33)	−2.7 (−38.2 to 53.0)[g]	.90
IL-6, pg/mL	0.38 (0.11)	0.51 (0.15)	−26.0 (−66.1 to 61.1)[g]	.45
NT-proBNP, pg/mL	431 (72)	543 (90)	−20.7 (−49.6 to 24.7)[g]	.31

Abbreviations: AF, atrial fibrillation; AFSS, Atrial Fibrillation Severity Scale; ATP, adenosine triphosphate; ECG, electrocardiogram; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; IL-6, interleukin 6; LA, left atrial; LDL-C, low-density lipoprotein cholesterol; LV, left ventricular; LVED, left ventricular end-diastolic; MRI, magnetic resonance imaging; NT-proBNP, N-terminal pro-brain natriuretic peptide; PCr, phosphocreatine; ^{31}P MRS, phosphorus-31 magnetic resonance spectroscopy; PPT, Physical Performance Test; RV, right ventricular; RVED, right ventricular end-diastolic; VAS, visual analog scale.

SI conversion factors: to convert cholesterol to mg/dL, divide by 0.0259; and triglycerides to mg/dL, divide by 0.0113.

[a] For the primary outcome, the secondary outcomes of body weight and PPT score, and quality-of-life VAS score, values shown are baseline-adjusted means (baseline-adjusted standard errors) estimated using analyses of covariance. For these outcomes, those with missing data at 8 months had their 4-month value used instead, or, if that was unavailable, their baseline value. Participants were classified as having nonzero AF burden if AF was detected on 14-day ECG monitoring or the 12-lead ECG at 8 months; otherwise, they were classified as zero AF burden. Ten participants lacked 8-month ECG data and were assumed to have nonzero AF burden in the main analysis. Excluding these participants yields zero AF burden proportions of 25/53 (47%) vs 29/55 (53%) (difference −5.6%, 95% CI, −26.2 to 15.1; *P* = .70). At 8 months, the median (IQR) change in weight from baseline was −9.8 (−13.9 to −6.0) kg in the low-calorie diet group and −2.7 (−6.7 to −0.4) kg in the control group. The median (IQR) change in body mass index (calculated as weight in kilograms divided by height in meters squared) from baseline was −3.0 (−4.6 to −1.6) and −0.8 (−2.6 to 0.1), respectively.

[b] Scores range from 0 to 35, with higher scores indicating more severe symptoms. We considered a difference of 4 points in AFSS symptom severity score as clinically relevant.[29]

[c] Scores range from 0 to 36, with higher scores indicating better physical performance.

[d] Scores range from 0 to 100, with higher scores indicating better perceived health status.

[e] Scores range from 3.25 to 30, with higher scores indicating greater overall burden of AF symptoms.

[f] For CRP, IL-6, and NT-proBNP, values shown are geometric means (with approximate SEs) and the between-group difference and its 95% CI represents a percentage difference between the geometric means (low-calorie diet/control). For IL-6, anyone with a value of 0 was reassigned the value 0.1 prior to these calculations.

[g] Percentage difference.

settings achieving more than 10% weight loss and follow-up durations exceeding 12 months.[34]

Limitations

This study has some limitations. First, it was an open-label trial. Nonetheless, outcome assessments were evaluated by observers blinded to treatment assignment and clinical information whenever feasible, reducing the risk of assessment bias. Second, trial initiation coincided with the onset of the COVID-19 pandemic, which disrupted recruitment and necessitated modifications to the original study procedures. As a result, some secondary and other assessments, including PPT, extended ambulatory ECG monitoring, blood sampling, and CMR imaging, could not be undertaken in all participants. Despite these constraints, follow-up for the primary end point was excellent, with low and balanced dropout across study groups. Third, the weight loss achieved was moderate, in keeping with a dietary and lifestyle intervention, rather than pharmacological weight loss[35] or bariatric surgery,[36] and this was insufficient to produce a significant improvement in blood pressure, lipid levels, or CRP levels in this cohort. Fourth, for secondary outcomes other than body weight, PPT score, and quality-of-life measures, follow-up values at 8 months were analyzed without baseline adjustment. When 8-month measurements were missing, baseline values were carried forward to maximize data completeness and preserve the intention-to-treat population. This approach was selected to ensure an adequate sample size for outcomes with heterogeneous data availability.

Conclusions

In older patients with overweight and persistent AF, a low-calorie diet and behavioral support program was associated with significant and sustained weight loss with no safety concerns but did not affect AF symptoms, AF burden, cardiac remodeling, or the need for further rhythm control interventions.

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