Impact of weight reduction on pericardial adipose tissue and cardiac structure in patients with atrial fibrillation

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Background Obesity and pericardial adipose tissue are independent risk factors for atrial fibrillation (AF) and adverse cardiac structural remodeling. The effect of weight reduction on pericardial adipose tissue and cardiac structure remains unknown.

Methods We prospectively performed cardiac magnetic resonance imaging on 87 participants with AF undergoing either structured weight management (intervention) or general lifestyle advice (control). We measured pericardial adipose tissue, atrial and ventricular volumes, and myocardial mass at baseline and 12 months.

Results In total, 69 participants underwent baseline and 12-month follow-up cardiac magnetic resonance imaging (intervention n = 36 and controls n = 33). From baseline to 12 months, weight loss (kg, mean [95% CI]) was greater in the intervention group from 101.5 kg (97.2-105.8 kg) to 86.5 kg (81.2-91.9 kg) as compared with controls from 102.6 kg (97.2-108.1 kg) to 98.7 kg (91.0-106.3 kg) (time-group interaction $P < .001$). The intervention group showed a reduction in left atrial volumes (mL) from 105.0 mL (98.9-111.1 mL) to 96.4 mL (91.6-101.1 mL), whereas the change in the control group was from 108.8 mL (99.6-117.9 mL) to 108.9 mL (99.8-118.0 mL) (time-group interaction $P < .001$). There was a decline in pericardial adipose tissue (cm^3) from 140.9 cm^3 (129.3-152.4 cm^3) to 118.8 cm^3 (108.1-129.6 cm^3) and myocardial mass (g) from 137.6 g (128.1-147.2 g) to 123.1 g (114.5-131.7 g) in the intervention group, whereas the change in the control group was from 143.2 cm^3 (124.6-161.7 cm^3) to 147.2 cm^3 (128.9-165.4 cm^3) for pericardial adipose tissue and 138.3 g (124.8-151.8 g) to 140.7 g (127.4-154.1 g) for myocardial mass (both variables, time-group interaction $P < .001$).

Conclusions Weight reduction results in favorable structural remodeling and a reduction in pericardial adipose tissue burden. (Am Heart J 2015;169:655-662.e2.)

Obesity is a significant risk factor for the development and progression of atrial fibrillation (AF).[1,2] We have recently demonstrated for the first time in a randomized trial that weight loss is associated with a reduction in AF burden in overweight and obese individuals.[3] The mechanisms by which weight loss results in reduction in AF burden remain uncertain, however.

Pericardial adipose tissue has recently emerged as a risk factor for the development of AF independent of traditional metabolic risk factors including measures of systemic obesity, such as body mass index (BMI).[4,5] Observations suggest that pericardial adipose tissue may be a unique metabolically active visceral adipose depot[6] and an important source of inflammatory and profibrotic cytokines, thereby potentially influencing contiguous cardiac pathologic changes. In the ventricular chambers, autopsy studies have shown a strong correlation between myocardial mass and pericardial adipose volume, independent of the underlying ventricular pathology, suggesting myocardial structural remodeling may, in part, be influenced by overlying pericardial adipose tissue.[7]

The aim of this current study was, therefore, to evaluate the effect of weight loss on pericardial adipose stores and cardiac structure in overweight/obese individuals with paroxysmal AF using cardiac magnetic resonance (CMR) imaging.

Methods

Study design and patient population

We recently reported the effect of weight and cardiometabolic risk management on the burden of AF

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in a randomized clinical trial of overweight/obese individuals attending the Center for Heart Rhythm Disorders of The University of Adelaide between June 2010 and December 2011 (anzctr.org.au identifier: ACTRN12610000497000).[3] This trial demonstrated that the weight management intervention resulted in a reduction in weight and in AF burden compared with controls. The current report is a CMR substudy of the primary trial. Of the 248 patients eligible for the primary study, 178 provided consent for participation. Of these, 91 patients were excluded from the CMR substudy (75 declined participation in the imaging sub study, and 16 had a contraindication to CMR). Thus, 87 participants entered the CMR substudy. Cardiac magnetic resonance was performed at the Cardiovascular Investigation Unit of The Royal Adelaide Hospital. Individuals with a BMI >27 kg/m^2; waist circumference >100 cm (male) or >90 cm (females), and aged 21-75 years with symptomatic paroxysmal or persistent nonvalvular AF (in sinus rhythm at enrolment) were eligible for study recruitment. Details of inclusion and exclusion criteria are detailed in online Appendix Supplementary Table I. Patients provided written informed consent to the study protocol, which was approved by the human research ethics committee of the Royal Adelaide Hospital and the University of Adelaide in accordance with the Declaration of Helsinki. No extramural funding was used to support this work. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final contents. All authors had access to the data and have approved the final article.

Outcomes

The study outcomes were the changes in CMR parameters between the 2 study groups over the 12-month period. The primary outcome was the change in pericardial adipose tissue volume, and the coprimary outcome was the change in atrial volumes. The secondary outcomes were the change in ventricular end-systolic and end-diastolic volumes and total myocardial mass.

Randomization and blinding

Randomization was performed in a 1:1 ratio by computer software (SPSS version 17, IBM Inc., Armonk, NY). The study was conducted as a partially blinded study. Study personnel involved in the analysis of outcomes including study coordinators and treating physicians were blinded to randomization, but by necessity, patients (who were instructed not to disclose their randomization status) and weight loss counselors were not blinded. Patient records contained general statements without indicating group allocation. Cardiac magnetic resonance analysis was performed by personnel who were blinded to participant group allocation.

Weight management

As previously described,[3] patients were randomized to either a structured weight management group or a control group.

The methodology is detailed in the online Appendix Supplementary material section. In brief, the intervention group underwent a 2-phase program using a physician-directed low calorie diet (LCD) (up to 1200 kcal/d), titrated exercise prescription, periodic supportive counseling, and nutritional behavioral coaching. The latter strategy was made the predominant focus for permanent lifestyle change, whereas the LCD was gradually weaned off. The control group was issued with 1-time written and verbal counseling regarding diet and exercise, in addition to 3 g/d of oral marine triglyceride supplementation (the latter for ethical trial design reasons).

Measurements

Weight and waist circumference measurement. Weight, height, BMI, and waist circumference were recorded using digital scales, a stadiometer and measuring tape, in accordance with standardized methods.

Blood pressure. Participants were instructed to measure blood pressure (BP) every morning and evening for 10 days using an automated monitor (Omron 5 series BP monitor; Omron Corporation, Kyoto, Japan), before each clinical review. In the seated position, patients were instructed to rest the right or left arm on a bench, at midchest level. A minimum of 2 recordings were taken and averaged if either systolic BP (SBP) or diastolic BP (DBP) values were within 5 mm Hg. Further measurements were taken if values were discrepant by >5 mm Hg. The mean morning and evening blood pressure for the preceding 10 days was calculated for that visit. Mean arterial blood pressure was calculated as DBP + 1/3 × (SBP − DBP).

CMR image acquisition. Cardiac magnetic resonance was performed using a 1.5T clinical magnetic resonance scanner (Avanto, Siemens, Erlangen, Germany) and a standard phased array surface coil with subjects in the supine position.

For the ventricular image set, long-axis reference views were used for positioning the 8-12 ventricular short-axis slices from the level of the mitral valve to left ventricular (LV) apex. Images were obtained during breath-hold (8-10 seconds) with retrospectively electrocardiogram–gated steady-state free precession sequences: image matrix 256 × 150, field of view 380 mm, repetition time 52.05 milliseconds, echo time 1.74 milliseconds, flip angle 70°. Standard ventricular short-axis slices were 6-mm thick with 4-mm intersection gaps.[8,9] For the atrial image set, contiguous slices in both short (biatrial) and

horizontal long-axis views (4 chambers) were obtained with slice thickness of 6 mm and no intersection gap.

Ventricular analysis

Ventricular analysis was performed offline using commercially available software (QMass v7.2, Medis, Leiden, Netherlands). Left ventricular and right ventricular (RV) chambers were manually traced at end diastole (start of R wave) and in end systole (smallest cavity area). Left ventricular basal slice selection was determined by at least 50% of ventricular myocardium surrounding the blood pool.[10] With regard to RV basal slices, as per previously published methods, only the volume below the level of the pulmonary valve was included.[11]

Atrial analysis

Atrial chambers were manually traced (Argus software, Siemens) using a short-axis disc summation method described previously at ventricular end systole and end diastole.[12] The borders of the left atrium were defined as the plane of the mitral valve and the visually apparent juncture of left atrium with pulmonary veins. The borders of the right atrium were defined as the plane of the tricuspid valve and the juncture with the caval veins.

Pericardial adipose tissue quantification

Pericardial adipose tissue was traced (Argus software, Siemens) at end diastole from the ventricular short-axis stack as described previously.[13] In summary, traces were made around the myoepicardial border and outermost border of adipose tissue, subtending an area of pericardial adipose tissue. Traces were undertaken on contiguous ventricular slices and pericardial adipose volume subsequently derived using a disc summation method.

Statistical analysis

Baseline demographic data are summarized using means and SD for continuous variables and proportions for categorical variables. For repeated measures analysis of continuous dependent variables, a linear mixed-effects model was used, with subject identity included as a random effect. Treatment group (ie, control vs intervention) was entered into the mixed model as a fixed effect, along with subjects' visit time and a group-time interaction term. If the interaction term was significant, then it was retained in the model, and it implied that the randomization group influence on the outcome variable was time dependent. Statistical tests were 2-sided, and a $P < .05$ was considered statistically significant. Power calculation was performed for AF symptom burden reduction in the larger cohort. For this imaging substudy, no a priori power calculations were performed for changes in pericardial fat or atrial volumes. All analyses were performed using STATA software, version 12.1 (Stata Corp, College Station, TX).

Results

The screening and enrolment of patients are illustrated in Figure 1. At 12-month follow-up, 69 of 87 recruited participants had undergone an interpretable follow-up scan; 12 declined repeat CMR, and 6 were excluded because of poor image quality. The baseline characteristics of the 69 participants are shown in Table I.

Weight reduction

Figure 2 presents the changes in anthropometric measures, mean arterial blood pressure, pericardial adipose tissue, and myocardial mass. In the control group, the mean weight (kg) (95% CI) had decreased from 102.6 kg (97.2-108.1 kg) at baseline to 98.7 kg (91.0-106.3 kg) at 12 months ($P = .01$). The intervention group achieved a greater weight reduction from 101.5 kg (97.2-105.8 kg) to 86.5 kg (81.2-91.9 kg) ($P < .001$), with the weight reduction being significantly greater in the intervention group (time-group interaction $P = .01$). Mean waist circumference (cm) decreased from 111.4 cm (107.5-115.4 cm) to 106.9 cm (100.9-112.9 cm) in the control group ($P = .002$). In the intervention group, waist circumference decreased from 111.0 cm (107.7-114.3 cm) to 96.2 cm (91.7-100.8 cm), $P < .001$ (time-group interaction $P = .004$). Mean arterial blood pressure (mm Hg) declined in the intervention group from 99 mm Hg (93-105 mm Hg) to 98 mm Hg (95-102 mm Hg) and 99 mm Hg (95-102 mm Hg) to 96 mm Hg (93-99 mm Hg) in the control group ($P = .05$ for time-group interaction).

Pericardial adipose tissue and myocardial mass

Table II and Figure 2 present the CMR changes in pericardial fat adipose tissue and myocardial mass.

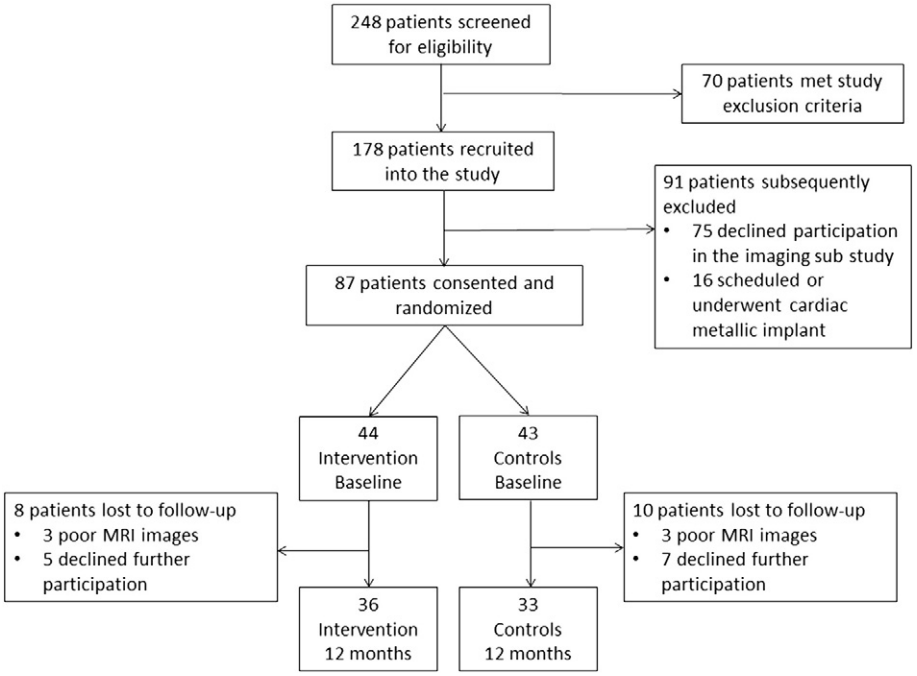
There was a significantly greater decline in pericardial adipose tissue (cm^3) in the intervention group as compared with the control group, $P < .001$ for time-group interaction. In conjunction, there was a significant decline in myocardial mass (g) in the intervention group, whereas the control group showed a small increase, time-group interaction $P < .001$.

After indexing myocardial mass to body height (g/m), the decline in height-indexed myocardial mass remained greater in the intervention group as compared with the control group (time-group interaction $P < .001$).

Cardiac chamber volumes

Table II and Figure 3 show the changes in atrial and ventricular volumes. Online Appendix Supplementary Table II presents the absolute change in chamber volumes in each group, from baseline to 12 months. End-diastolic (maximal) left atrial (LA) volume (mL) declined in the intervention group to a greater extent than the control group, time-group interaction $P < .001$. Similarly, there was a greater decline in end-diastolic right atrial (RA) volume (mL) in the intervention group as

Figure 1



Patient flow.

Table I. Baseline characteristics

	Control group (n = 33)	Intervention group (n = 36)
Age (y)	59 ± 11	60 ± 9
Gender, n (%)		
Male	21 (64)	26 (72)
Female	12 (36)	10 (28)
AF type, n (%)		
Paroxysmal	20 (61)	22 (61)
Persistent	13 (39)	14 (39)
Weight (kg)	102.6 ± 15.4	101.5 ± 12.7
Waist circumference (cm)	111.4 ± 11.1	111.0 ± 9.8
BMI (kg/m)	33.9 ± 3.7	32.6 ± 3.5
Hypertension n (%)	28 (85)	30 (83)
Diabetes or IGT, n (%)	9 (27)	7 (19)
Hyperlipidemia, n (%)	23 (70)	20 (56)
Coronary artery disease, n (%)	5 (15)	2 (6)
Valve disease, n (%)	0	2 (6)
Excess alcohol consumption, n (%)	13 (39)	12 (33)
Tobacco use, n (%)		
Current	2 (6)	1 (3)
Never	19 (58)	23 (64)
Reformed	12 (36)	12 (33)

Categorical variables are presented as proportions, and continuous variables are presented as mean and SD.
Abbreviation: *IGT*, Impaired glucose tolerance.

compared with the control group, time-group interaction $P < .001$. The greater decline observed in the intervention group, as compared with controls, was also seen for end-systolic (minimal) LA and RA volumes (time-group interaction $P = .004$ and $P = .007$ for systolic LA and RA volumes, respectively). In addition, after indexing atrial volumes to body height, the observed decline in the intervention group atrial volumes remained significantly greater than for the controls, time-group interaction $P < .001$ for both height-indexed LA and RA volumes. No significant changes were observed between the groups with respect to end–diastolic and end-systolic LV and RV volumes (Table II and Figure 3).

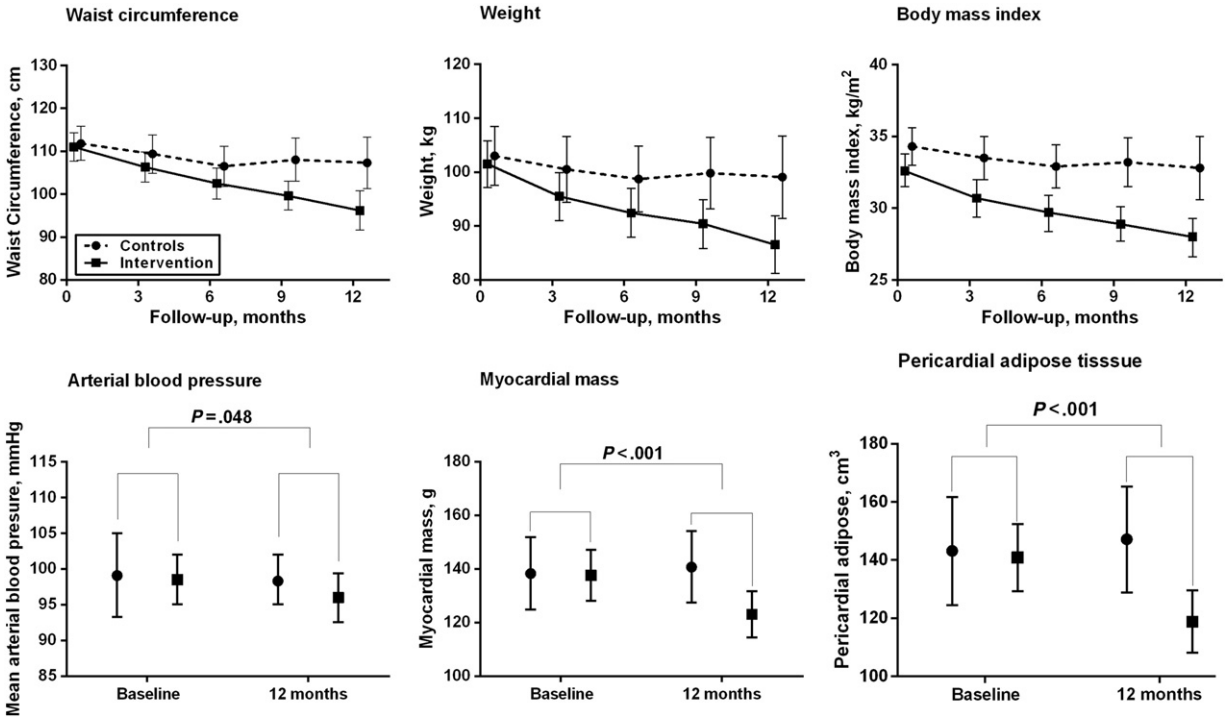
Discussion

The main findings from this CMR study were that a weight loss intervention resulted in greater weight loss compared with controls, which was accompanied by significant reduction in pericardial adipose tissue, atrial volumes, and myocardial mass.

Pericardial adipose tissue

Pericardial adipose tissue is composed of 2 components, epicardial (visceral) fat layer and paracardial (mediastinal), the latter is external to the parietal pericardial tissue.[13] Pericardial adipose tissue has been

Figure 2



Changes in anthropometric measures, pericardial adipose volume, and myocardial mass.

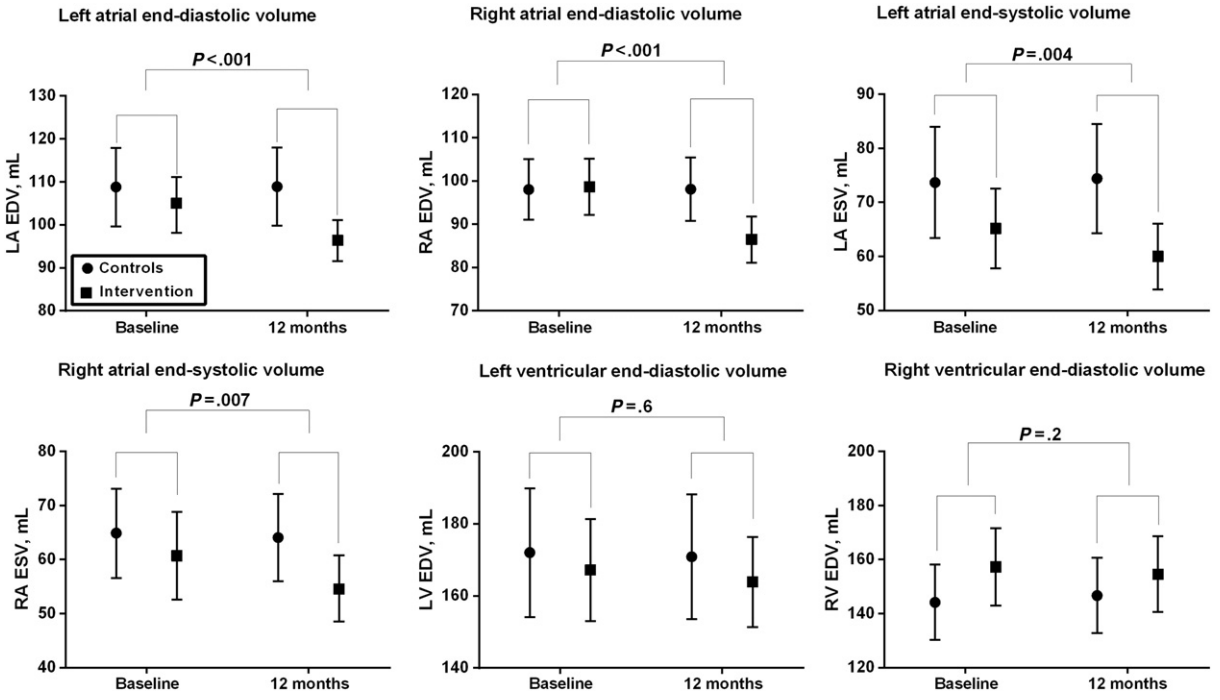
Table II. CMR imaging changes

	Control (n = 33)			Intervention (n = 36)			
	Baseline	12 m	*P**	Baseline	12 m	*P**	*P*†
LV EDV (mL)	167 (133-193)	166 (128-197)	.69	167 (133-199)	167 (134-192)	.27	.6
LV ESV (mL)	49 (38-71)	47 (37-68)	.20	44 (33-62)	43 (35-55)	.55	.8
RV EDV (mL)	148 (106-172)	152 (105-172)	.42	150 (130-187)	147 (12-182)	.36	.2
RV ESV (mL)	52 (42-77)	48 (42-73)	.44	54 (41-73)	55 (40-69)	.19	.4
Myocardial mass (g)	136 (113-162)	143 (118-164)	.05	134 (118-165)	117 (107-142)	<.001	<.001
Myocardial mass indexed (g/m)	78 (65-92)	82 (66-91)	.04	76 (68-88)	66 (61-76)	<.001	<.001
LA EDV (mL)	111 (85-128)	112 (86-128)	.74	105 (91-119)	98 (88-105)	<.001	<.001
LA EDV indexed (mL/m)	62 (50-72)	62 (50-70)	.66	60 (52-65)	55 (50-60)	<.001	<.001
LA ESV (mL)	68 (51-93)	67 (51-93)	.08	62 (48-84)	60 (47-71)	.008	.004
RA EDV (mL)	98 (77-115)	100 (78-112)	.89	98 (88-105)	83 (75-97)	<.001	<.001
RA EDV indexed (mL/m)	58 (47-62)	57 (47-62)	.93	58 (47-62)	48 (43-56)	<.001	<.001
RA ESV (mL)	62 (47-82)	62 (47-82)	.03	55 (41-75)	52 (40-62)	.002	.007
Pericardial adipose tissue (cm^3)	130 (106-184)	128 (107-189)	.002	136 (119-171)	115 (93-134)	<.001	<.001

Data are presented as mean and 95% CI. Chamber volumes are presented in milliliters (mL) and pericardial fat in cubic centimeters (cm^3). Measurements are presented as absolute and indexed to height (m).
Abbreviations: *LV EDV*, Left ventricular end-diastolic volume; *LV ESV*, left ventricular end-systolic volume; *RV EDV*, right ventricular end-diastolic volume; *RV ESV*, right ventricular end-systolic volume; *LA EDV*, left atrial end-diastolic volume; *LA ESV*, left atrial end-systolic volume; *RA EDV*, right atrial end-diastolic volume; *RA ESV*, right atrial end-systolic volume.
* *P* values represent the level of significance for the change from baseline to 12 months in each group.
† *P* values represent the level of significance for time-group interaction.

recognized as a novel risk factor for incident AF and its chronicity and severity.[14] In addition, increased pericardial adipose tissue has been associated with worse catheter ablation outcomes.[4] The present study has demonstrated a significant reduction in pericardial adipose tissue after a structured weight loss intervention. Although a correlation between pericardial adipose tissue and other traditional measures of obesity such as BMI, waist circumference, and visceral adipose tissue is to be expected,[15,16] there is emerging evidence that pericardial adipose tissue has some

Figure 3



Changes in atrial and ventricular volumes.

unique determinants and effects. Snel et al[17] recently demonstrated reduction of pericardial adipose tissue via a LCD. Importantly, the reduction in pericardial adipose tissue volume persisted despite subsequent body weight and abdominal visceral adipose tissue re-gain. This observation suggests that changes in pericardial adipose tissue burden do not appear to parallel changes in visceral adiposity. Epicardial adipose tissue has been shown to be a local source of proinflammatory and profibrotic mediators.[18] Areas of myocardial fibrosis have been localized to areas subtended by epicardial adipose pads, suggesting a paracrine mechanism influencing atrial structure, electrical function,[19] and subjacent chamber geometry.[20]

The current study demonstrates that weight loss intervention is associated with a reduction in pericardial fat volume and atrial volumes. Previously, we have shown that weight loss is associated with a reduction in AF burden.[3] Taken together, these observations lend support to the hypothesis that pericardial adipose tissue is a mediator of AF, although this hypothesis needs further evaluation in clinical trials.

Atrial reverse structural remodeling

In this trial, the weight loss intervention resulted in a significant reduction in RA and LA volumes. Left atrial enlargement is strongly associated with AF in both obese and nonobese individuals,[21-23] so the reduction in LA volume observed is also consistent with our previous finding of reduced AF burden with a weight management intervention. Obesity may be associated with LA enlargement by several mechanisms. Obesity has been implicated in atrial fibrosis,[24] hypertension,[25] and obstructive sleep apnea,[26] which are also associated with atrial dilatation.[23,24] Although this study is the first to demonstrate in a randomized trial that a weight loss intervention mitigates adverse LA structural remodeling, the rapidity of this reverse structural remodeling is surprising. We speculate that, had LA dilatation been principally caused by atrial fibrosis, a significant reduction in LA volume in 12 months might not have been observed. We therefore postulate that reversible atrial stretch likely precedes a more irreversible fibrotic stage of atrial structural remodeling. Neurohormonal activation and plasma volume expansion resulting in elevated preload may account for RA hypertension and dilation. Importantly, sleep-disordered breathing and abnormalities of pulmonary vascular pressure are often associated with obesity. The observed reverse structural remodeling in RA volume may reflect amelioration of obesity-associated respiratory abnormalities.

Myocardial mass regression

Myocardial hypertrophy is an adaptive hemodynamic response to pressure and volume overload in obese patients.[27,28] Myocardial wall stress induces myocyte hypertrophy and a reactive fibrosis. The amenability of

LV hypertrophy regression with pharmacologic intervention has been demonstrated.[29] Exercise has been shown to reduce echocardiographic ventricular hypertrophy in overweight hypertensive subjects.[30] In the present study, the intervention group showed a significant decrease in myocardial mass with weight and SBP reduction, although with no significant change in systolic or diastolic ventricular volumes. Obese patients have been shown to be predisposed to hypertrophic cardiac steatosis and diastolic dysfunction, which are reversible with caloric restriction, weight loss, and glucoregulation.[31] The finding of reduced myocardial mass in the intervention group in our study is consistent with this previous evidence.

Limitations

The study patient population was small, and the study was conducted primarily in a male white population with nonvalvular AF, hence limiting generalizability in other patient groups. A further limitation in our study is the number (18 of 87, 20%) of patients who did not undergo repeat CMR. Patient retention in weight loss studies is a challenging task. A systematic review[32] illustrated the scope of the problem by estimating a 67% loss to follow-up at 12 months. In our cohort, a 20% attrition rate is relatively modest. Gadolinium was not administered as part of the CMR protocol, so evaluation of myocardial fibrosis is not possible. Administration of omega-3 marine triglycerides to the control group may have confounded the effect, the differences in arrhythmia burden, cardiac dimensions, and visceral adiposity between the groups. However, although these fatty acids have been shown to stabilize myocardial electrical membranes and prevent calcium overloading,[33] recent data have been inconclusive.[34,35] Although we cannot exclude a confounding effect, it is likely that omega-3 oil supplementation in the control group had a neutral effect. Finally, the exclusion of individuals with systolic heart failure means that the study findings cannot be necessarily generalized to individuals with systolic heart failure.

Conclusions

In patients with paroxysmal and persistent AF, a structured weight management program results in a reduction in pericardial adipose tissue and favorable changes in cardiac structure.

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Appendix

Supplementary Table I. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Patients 21-75 years of age	Serious underlying medical disorder: eg, malignancy, chronic uncontrolled autoimmune or inflammatory disorder
Patients with paroxysmal or persistent AF, in sinus rhythm at the time of recruitment	Serious underlying psychiatric disorder: eg, eating disorder, severe psychotic disorder with recent (3 m) hospitalization or psychiatric illness requiring supervised care precluding full independent function; patients unable to provide informed consent
	Recent weight loss program participation: recent (3 m) participation in a weight loss program, either commercial or medically supervised
	Gastrointestinal malabsorption disorder: a previously diagnosed gastrointestinal malabsorption disorder interfering with macronutrient or micronutrient absorption
	Unstable INR: elevated INR (supratherapeutic INR and concomitant bleeding or elevated INR requiring hospitalization for pharmacologic reversal administration); persistently subtherapeutic INR (<2.0 for ≥14 consecutive days) in a patient with a $CHADS_2$ thromboembolic risk score ≥2
	The presence of diabetes mellitus (either autoimmune or adult onset, necessitating insulin therapy
	Moderate or severe cardiac valvular lesion (stenosis or regurgitation) on echocardiography or valvular lesion requiring intervention
	Diagnosed endocrinopathy: including subclinical thyroid disease (isolated abnormal serum thyrotropin levels)
	Current documented intracardiac thrombi on transesophageal echocardiography
	Age >75 years or <18 years or women of childbearing age
	Active or recent (within 6 m) cardiac ischemia
	Active gout or history of recurrent gout in the absence of prophylactic therapy
	Previous or active gallbladder disease

Abbreviations: *INR*, International normalized ratio; $CHADS_2$, specifies the composite thromboembolic risk in AF where C is cardiac failure (1), H is hypertension (1), A is age >75 (1), D is diabetes (1), and S is stroke or transient ischemic attack (2).

Weight management methodology

Intervention group

The structured weight loss program consisted of 2 phases, weight loss phase (phase 1) and weight maintenance phase (phase 2).

Phase 1

This comprised an 8-week modified LCD period followed by a 13-month low glycemic index meals maintenance period. Patients were prescribed LCD meal replacement sachets (Prima Health Solutions, Frenchs Forest, New South Wales, Australia) for 2 of their daily meals. The third meal consisted of a high animal and plant protein, low glycemic index, calorie-controlled meal, with a total of 800-1200 kcal/d.

Phase 2

This occupied the remainder of the 15-month period, whereby LCD meal supplements were gradually phased out, and emphasis focused on education for permanent lifestyle change. Nutritional behavioral change was encouraged primarily via problem solving, nutritional decision coaching, incremental goal setting, nutritional behavioral reflection, reinforcement, and self efficacy.

Motivational and goal-directed face-to-face visits 20-40 minutes in duration were scheduled every 3 months, where anthropometric measurements and a review of the lifestyle journal were undertaken. Additional visits were scheduled by the participant at will, and 24-hour e-mail and telephone contact was provided for additional support when required.

Control group

Standard care (control) group participants were issued with once off written and verbal advice regarding health nutrition and exercise guidelines at commencement of their participation. Weight management was a self–directed process. Follow-up was scheduled every 3 months as for the intervention group. As control patients were not provided with any structured supervised weight management or exercise program, from an ethical perspective, it was deemed appropriate to provide this group with 3 g/d of oral omega-3 marine triglyceride supplements with the aim of optimizing lipid profiles and overall cardiovascular risk. At the time of formulating the study protocol, preliminary evidence was suggestive of cardiovascular risk benefit with the use of marine triglycerides.[36,37]

Lifestyle journal and physical activity

Participants in the intervention group were required to maintain a self-monitoring lifestyle journal detailing food

Supplementary Table II. Changes in chamber volumes in each group from baseline to 12 months

	Control (n = 33)	Intervention (n = 36)	*P*
LV EDV (mL)	1.2 (−4.7 to 7.0)	3.3 (−2.6 to 9.2)	.6
LV ESV (mL)	1.4 (−0.8 to 3.6)	1.0 (−2.3 to 4.3)	.8
RV EDV (mL)	−2.5 (−8.6 to 3.7)	2.7 (−3.2 to 8.6)	.2
RV ESV (mL)	0.7 (−1.1 to 2.4)	2.0 (−1.0 to 5.1)	.4
Myocardial mass (g)	−2.4 (−4.8 to 0)	14.5 (12.1 to 16.9)	<.001
Myocardial mass indexed (g/m)	−1.4 (−2.8 to −0.1)	8.2 (6.9 to 9.4)	<.001
LA EDV (mL)	−0.2 (−1.1 to 0.8)	8.7 (5.7 to 11.6)	<.001
LA EDV indexed (mL/m)	−0.1 (−0.6 to 0.4)	4.9 (3.2 to 6.5)	<.001
LA ESV (mL)	−0.7 (−1.5 to 0.1)	5.2 (1.5 to 9.0)	.004
RA EDV (mL)	−0.1 (−1.4 to 1.2)	12.2 (9.0 to 15.4)	<.001
RA EDV indexed (mL/m)	0 (−0.8 to 0.7)	6.8 (5.1 to 8.6)	<.001
RA ESV (mL)	0.7 (0.1 to 1.4)	6.1 (2.4 to 9.7)	.007
Pericardial adipose tissue (cm^3)	−4.0 (−6.5 to −1.6)	136 (119 to 171)	<.001

Data are presented as mean and 95% CI. *P* values represent the level of significance for the change from baseline to 12 months between groups. Chamber volumes presented in milliliters (mL) and pericardial fat in cubic centimeters (cm^3). Measurements are presented as absolute and indexed to height (m).
Abbreviations: *LV EDV*, Left ventricular end-diastolic volume; *LV ESV*, left ventricular end-systolic volume; *RV EDV*, right ventricular end-diastolic volume; *RV ESV*, right ventricular end-systolic volume; *LA EDV*, left atrial end-diastolic volume; *LA ESV*, left atrial end-systolic volume; *RA EDV*, right atrial end-diastolic volume; *RA ESV*, right atrial end-systolic volume.

type and quantity. Exercise was prescribed initially at 20 minutes of low intensity thrice weekly and titrated over phase 1 to reach 45 minutes thrice weekly. This was maintained over phase 2, with the substitution of 1 low-intensity activity with at least 1 moderate-intensity activity per week. Type of activity and duration was logged into the journal. Control group participants were not required to maintain a lifestyle journal, and education regarding activity levels was issued in the form of specific written material.

Supplementary references

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