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ORIGINAL INVESTIGATIONS

Long-Term Changes in Cardiac Structure and Function Following Bariatric Surgery

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ABSTRACT

BACKGROUND Studies with short-term follow-up have demonstrated favorable effects of weight loss (WL) on the heart, but little information is available regarding long-term effects or effects of visceral fat reduction.

OBJECTIVES The purpose of this study was to evaluate the effects of long-term WL following bariatric surgery on cardiac structure, function, ventricular interaction, and body composition, including epicardial adipose thickness and abdominal visceral adipose tissue (VAT).

METHODS A total of 213 obese patients underwent echocardiography before and >180 days following bariatric surgery. Abdominal VAT area was measured by computed tomography in 52 of these patients.

RESULTS After 5.3 years (IQR: 2.9-7.9 years), body mass index (BMI) decreased by 22%, with favorable reductions in blood pressure, fasting glucose, and left ventricular (LV) remodeling in the full sample. In the subgroup of patients with abdominal computed tomography, VAT area decreased by 30%. In all subjects, epicardial adipose thickness was reduced by 14% (both $P < 0.0001$) in tandem with reductions in ventricular interdependence. LV and right ventricular longitudinal strain improved following WL, but left atrial (LA) strain deteriorated, while LA volume and estimated LA pressures increased. In subgroup analysis, LV wall thickness and strain correlated more strongly with VAT than BMI at baseline, and reductions in LV mass following surgery were correlated with decreases in VAT, but not BMI.

CONCLUSIONS In this observational study, weight loss following bariatric surgery was associated with epicardial fat reduction, reduced ventricular interaction, LV reverse remodeling, and improved longitudinal biventricular mechanics, but LA myopathy and hemodynamic congestion still progressed. Reduction in visceral fat was associated with favorable cardiac effects, suggesting this might be a key target of WL interventions. (J Am Coll Cardiol 2022;80:1501–1512)

The prevalences of both obesity and heart failure with preserved ejection fraction (HFpEF) are increasing to epidemic proportions.[1,2] Obesity, especially when linked to increases in visceral fat, has deleterious effects on the cardiovascular system and is strongly tied to development and severity of HFpEF.[3,4] Excess body weight (BW) in patients with the obese phenotype of

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ABBREVIATIONS AND ACRONYMS

BMI = body mass index

BW = body weight

EAT = epicardial adipose tissue

eFS = endocardial fractional shortening

FWLS = free wall longitudinal strain

GLS = global longitudinal strain

HF = heart failure

HFpEF = heart failure with preserved ejection fraction

LA = left atrial

LV = left ventricular

RV = right ventricular

RWT = relative wall thickness

SAT = subcutaneous adipose tissue

VAT = visceral adipose tissue

WL = weight loss

HFpEF is associated with greater cardiac hypertrophy, abnormal myocardial energetics, heightened pericardial restraint, and hemodynamic congestion that is more strongly linked to volume expansion and alterations in venous capacitance.[4-7] These findings suggest that weight loss (WL) may improve these pathophysiologic components.

Modest WL via caloric restriction reduced left ventricular (LV) mass and improved exercise capacity in patients with obesity and HFpEF.[8] Effects on cardiac function were minimal, but the treatment duration was short, and the degree of WL achieved was modest. Bariatric surgery produces more robust and sustained WL, is associated with decreased risk of new-onset heart failure (HF),[9] and has been associated with LV and left atrial (LA) reverse remodeling in short-term studies.[10-13] However, very little is known regarding chronic effects of WL on the heart (>3 years), and existing literature is limited by smaller, highly selected studies, variable selection criteria and imaging techniques, and inconsistent breadth of cardiac and body composition assessments.

The present study aimed to fill these gaps by evaluating the relationships among general adiposity; regional fat distribution; and cardiac structure, function, and ventricular interaction among obese adults without HF before and following bariatric surgery, with much longer follow-up duration than previously reported.

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METHODS

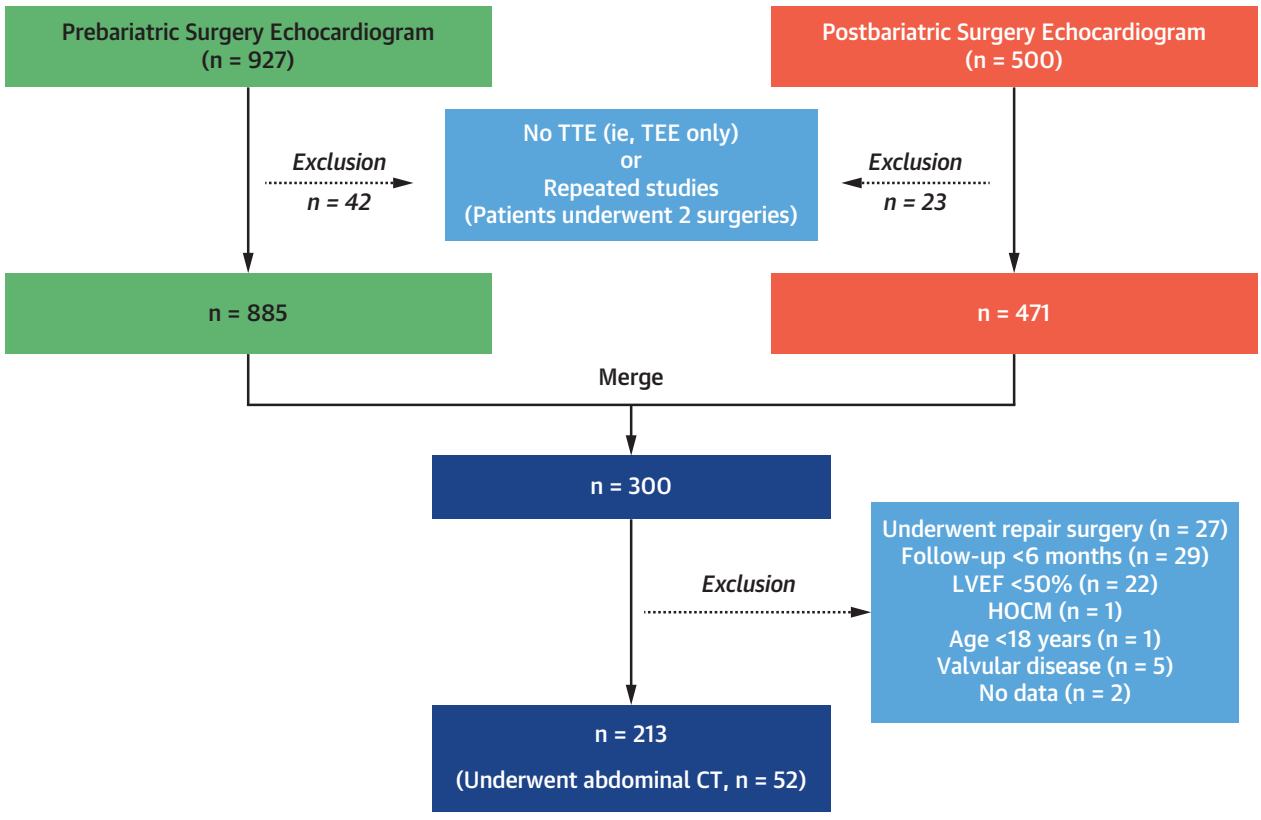
STUDY POPULATION. This is a retrospective, observational cohort study evaluating consecutive adults who underwent bariatric surgery (including open and endoscopic surgeries) at the Mayo Clinic between January 2008 and December 2017. Patients who underwent an echocardiographic evaluation before and >180 days following bariatric surgery were included in the analysis to evaluate longitudinal changes. If a patient had multiple postsurgery echocardiograms, the most recent study (distant from examination 1) was used as examination 2. Exclusion criteria included patients who underwent repair surgery and those with any history of left ventricular ejection fraction (LVEF) <50%, primary cardiomyopathy, or moderate or greater valve disease. Of these patients, 52 underwent abdominal computed tomography before and after bariatric surgery within 12 months of echocardiography. Informed written consent was obtained from all patients to utilize their data, and the study was approved by the Mayo Clinic Institutional Review Board.

ECHOCARDIOGRAPHIC ASSESSMENT OF CARDIAC STRUCTURE AND FUNCTION. Two-dimensional (2D), M-mode, Doppler, and tissue Doppler echocardiography was performed prebariatric surgery and postbariatric surgery according to the guidelines of the American Society of Echocardiography.[14] LV mass was indexed to height$^{2.7}$.[4,6] Relative wall thickness (RWT) was defined as the ratio of twice LV diastolic posterior wall thickness to the LV end-diastolic dimension. LV end-diastolic volume, end-systolic volume, and LVEF were determined using the Teichholz method. Endocardial fractional shortening (eFS) was determined from 2D systolic and diastolic dimensions. LV diastolic function was assessed using the early diastolic mitral inflow velocity (E), the early diastolic septal mitral annular tissue velocity (e'), and the ratio of E/e'. Left atrial (LA) volume was determined using the biplane method of disks.

Right ventricular (RV) basal, midcavity, and longitudinal dimensions were measured at end-diastole using RV-focused views. RV fractional area change was measured as an endocardial-based metric of RV systolic function.[14] Myocardial deformation analyses were performed off-line, using commercially available software (Image Arena, Tom Tec Imaging Systems). LV global longitudinal strain (GLS) was measured using 2D speckle tracking. LVGLS was determined as the average of the 3 apical views. LA reservoir function was evaluated by peak LA strain during LA relaxation, using the QRS complex of electrocardiogram as the fiducial point. RVGLS and RV free wall longitudinal strain (FWLS) were obtained from the apical 4-chamber view.[15] Strain data are presented as absolute values because the direction of tissue motion during systole is self-evident. Echocardiographic and abdominal computed tomography (CT) measurements were performed prospectively on existing images that were obtained during the predefined study interval by an experienced investigator who was blinded to patient information and the time point of the examination.

ASSESSMENT OF ADIPOSE DEPOTS AND VENTRICULAR INTERACTION. Epicardial adipose tissue thickness (EAT) was measured perpendicularly to the free wall of the RV by echocardiography in the parasternal long-axis view.[16] Total heart volume was estimated from 2 hemi-ellipsoids containing both atria and

FIGURE 1 **Patient Identification**



Flow diagram outlining patient exclusions to qualify for inclusion to arrive at the final sample of 213 patients with repeat assessments before and following bariatric surgery. CT = computed tomography; HOCM = hypertrophic obstructive cardiomyopathy; LVEF = left ventricular ejection fraction; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

ventricles with the apical 4-chamber view.[17] Ventricular interdependence was quantified in the parasternal short-axis view on 2D echocardiography by the LV eccentricity index and using planimetry to calculate idealized and actual LV radii (ideal/actual radius), whereby higher values of both indexes indicated greater septal flattening, enhanced ventricular interdependence, and increased pericardial restraint.[6,16]

Among participants that underwent abdominal computed tomography scans for clinical indications within 12 months of echocardiography, abdominal visceral adipose tissue (VAT) area was measured at the L3 level based on the tomographic cross-sectional areas, as previously described (Supplemental Methods 1, Supplemental Figure 1).[4,18] The reader was blinded to the patient information and the time point of the examination.

The reliability and reproducibility of echocardiographic variable measurement was assessed in 20 randomly selected patients. Intraobserver agreement was evaluated after the same observer repeated the measurements 4 weeks later, and interobserver agreement was tested by comparing the measurement made by another experienced reader. The intraclass correlation coefficients for intraobserver and interobserver agreement were strong (all 0.72-0.95) (Supplemental Table 1).

STATISTICAL ANALYSIS. Data are presented as mean ± SD, median (IQR), or n (%). Within-group differences were assessed using paired Student's *t*-test, Wilcoxon matched-pair signed rank test, or McNemar test as appropriate. Between-group differences were compared using the unpaired Student's *t*-test, Wilcoxon rank sum test, chi-square, or Fisher exact test as appropriate. Pearson's or Spearman's correlation analysis was used to assess the relationships between continuous variables. Differences of correlation coefficients were assessed using a Meng's

TABLE 1 Baseline Characteristics

Age, y	54 ± 11
Female	143 (67)
Height, cm	167 ± 10
Body weight, kg	128 ± 30
Body mass index, kg/m^2	43 (39-50)
Surgical form	
Gastric bypass and Roux-en Y gastrectomy	121 (57)
Longitudinal gastrectomy	48 (22)
Placement of gastric band	12 (6)
Biliopancreatic division with duodenal switch	27 (13)
Gastric bypass and small intestine reconstruction	5 (2)
Comorbidities	
Hypertension	161 (76)
Coronary artery disease	39 (18)
Atrial fibrillation	35 (16)
Diabetes mellitus	87 (41)
Dyslipidemia	126 (59)
Obstructive sleep apnea	151 (71)
HFpEF	11 (5)
Medications	
ACE inhibitor or ARB	98 (46)
Beta-blocker	89 (42)
Calcium-channel blocker	40 (19)
Diuretic agents	101 (47)
Laboratories	
Hemoglobin, mg/dL	13.6 ± 2.6
eGFR, mL/min/1.73 m^2	55 ± 22
Fasting glucose, mg/dL	110 (98-132)
HbA_{1c}, %	6.0 (5.5-7.2)

Values are mean ± SD, n (%), or median (IQR).

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; eGFR = estimated glomerular filtration rate; HbA_{1c} = glycosylated hemoglobin; HFpEF = heart failure with preserved ejection fraction.

Z-test. A 2-sided P value <0.05 was considered statistically significant. All data were analyzed using JMP14.0 (SAS Institute Inc).

RESULTS

SUBJECT CHARACTERISTICS. A total of 213 patients met inclusion criteria (Figure 1). The average age was 54 ± 11 years, average body mass index (BMI) was 45 ± 10 kg/m^2, and 67% of the patients were women. Patients displayed typical comorbidities associated with obesity, including high prevalence of hypertension, diabetes mellitus, dyslipidemia, and obstructive sleep apnea (Table 1). A minority (5%) of patients had history of clinically diagnosed HFpEF. Of 213 patients, 52 patients underwent serial abdominal CT scan. Patients referred for abdominal CT displayed lower hemoglobin, but other baseline characteristics were similar to patients not referred for CT (Supplemental Table 2). VAT area and subcutaneous adipose tissue (SAT) area were measured in this subset of 52 subjects; the average VAT area was 301 ± 129 cm^2, and the average SAT area was 505 ± 191 cm^2 (Table 2).

BASELINE CARDIAC STRUCTURE AND FUNCTION. At examination 1, patients displayed increased LV mass and RWT indicating concentric remodeling (Table 3). In the total population, 71% of the patients showed LV systolic dysfunction assessed by LVGLS and 34% of the patients showed RV systolic dysfunction assessed by RVFWLS (Table 3). Among the population with abdominal CT, LV mass was correlated with VAT area (r = 0.52; P < 0.0001); but it was not correlated with SAT area (r = −0.01; P = 1.00) (Figure 2). RWT correlated positively with VAT area (r = 0.48; P = 0.001) but did not correlate with BW or BMI. LV interventricular septal dimension and posterior wall dimension had stronger correlations with VAT area (r = 0.61; P < 0.0001 and r = 0.61; P < 0.0001) compared with BW (r = 0.36; P < 0.0001 and r = 0.34; P < 0.0001) or BMI (r = 0.20; P = 0.007 and r = 0.17; P = 0.02) (all comparisons of R coefficient were P < 0.05) (Figure 2). These findings were also confirmed restricting the analysis to include only patients with VAT assessment (Supplemental Figure 2). LVGLS correlated inversely with VAT area (r = −0.31; P = 0.047). RVGLS also correlated negatively with VAT area (r = −0.36; P = 0.04) but did not correlate with BW or BMI (Figure 2).

EFFECTS OF WEIGHT LOSS ON BODY COMPOSITION, METABOLISM, AND COMORBIDITIES. The median duration between examinations 1 and 2 in the study population was 5.3 years (IQR: 2.9-7.9 years). Follow-up duration was not significantly different between the subgroups with and without abdominal CT (4.5 years [IQR: 3.0-7.5 years] vs 5.4 years [IQR: 2.9-8.1 years]; P = 0.50). BW was reduced by 23%, and BMI showed a mean 22% reduction overall (Table 3 and Figure 3A). In the subgroup of patients with abdominal CT, both VAT area and SAT area significantly decreased by 30% and 29% from the baseline. Among the overall population, epicardial adipose tissue thickness was reduced by 14%. Estimated plasma volume decreased in tandem with the WL. Similar findings were also observed in the analysis restricted to patients with VAT assessment (Supplemental Figure 3).

A decrease in the levels of fasting glucose and HbA_{1c} were observed, suggesting improved insulin sensitivity. Heart rate and blood pressure decreased, despite no change in use of antihypertensive medicines, and a decrease in diuretic usage from examination 1 to 2, mirroring the decrease in estimated plasma volume (Table 3). The prevalences of diabetes and obstructive sleep apnea decreased following

TABLE 2 Longitudinal Changes in Body Composition and Cardiometabolic Risk Factors

	Examination 1	Examination 2	*P* Value Examination 1 vs 2	Change From Baseline
Follow-up duration, y		5.3 (2.9-7.9)		
Body composition				
Body height, cm	168 ± 10	167 ± 10	<0.0001	−1.0 ± 3.3
Body weight, kg	123 (106-141)	93 (80-110)	<0.0001	−31 ± 25
Body mass index, kg/m^2	43 (39-50)	33 (29-39)	<0.0001	−11 ± 9
VAT area, cm^2 (n = 52)	296 (216-394)	175 (94-302)	<0.0001	−92 ± 117
SAT area, cm^2 (n = 52)	483 (367-617)	309 (224-400)	<0.0001	−176 ± 181
Estimated plasma volume, mL (n = 195)	4,018 (3,497-4,664)	3,289 (2,899-3,728)	<0.0001	−785 ± 744
Estimated plasma volume/BSA, mL/m^2 (n = 195)	1,757 (1,644-1,498)	1,638 (1,519-1,764)	<0.0001	−157 ± 221
Comorbidities				
Hypertension	161 (76)	156 (73)	0.40	−5 (−3%)
Diabetes	87 (41)	49 (23)	<0.0001	−38 (−18%)
Obstructive sleep apnea	151 (71)	115 (54)	<0.0001	−36 (−17%)
Atrial fibrillation	35 (16)	48 (23)	0.0003	+13 (+7%)
HFpEF	11 (5)	20 (9)	0.003	+9 (+4%)
Medications				
ACE inhibitor or ARB	98 (46)	92 (43)	0.29	−6 (−3%)
Beta-blocker	89 (42)	85 (40)	0.48	−4 (−2%)
Calcium-channel blocker	40 (19)	39 (18)	0.79	−1 (−1%)
Diuretic agents	101 (47)	83 (39)	0.003	−18 (−8%)
Laboratories				
eGFR, mL/min/1.73 m^2 (n = 195)	55 ± 22	56 ± 24	0.29	1.4 ± 18.2
Fasting glucose, mg/dL (n = 187)	110 (98-132)	106 (90-114)	<0.0001	−15 ± 36
HbA_{1c}, % (n = 159)	6.0 (5.5-7.2)	5.6 (5.1-6.6)	<0.0001	−0.6 ± 1.3
Hemodynamics				
Systolic BP, mm Hg	131 ± 19	125 ± 20	0.0006	−6 ± 23
Diastolic BP, mm Hg	75 ± 11	72 ± 12	0.0003	−4 ± 14
Heart rate, beats/min	72 (64-82)	68 (60-78)	0.002	−4 ± 18

Values are median (IQR), mean ± SD, or n (%). Sample size with available data shown in column 1 for assessments not available in all participants.
BP = blood pressure; BSA = body surface area, SAT = subcutaneous adipose tissue; VAT = visceral adipose tissue; other abbreviations as in Table 1.

surgery, but the prevalences of both atrial fibrillation and HFpEF both increased, despite marked weight reduction (Table 2).

LONGITUDINAL CHANGES IN THE LV FOLLOWING WEIGHT LOSS. LV mass decreased because of a reduction in the LV wall thickness without a change in the LV diastolic dimension, and both cardiac output and stroke volume decreased following WL in tandem with the reduction in body weight and estimated plasma volume (Table 3). Changes in LV mass were correlated with change in VAT area ($r = -0.43$; $P = 0.004$) (Figure 3B), but were not correlated with changes in SAT area ($r = 0.05$; $P = 0.80$) or with changes in EAT ($r = 0.06$; $P = 0.40$).

Modest but significant reductions in systolic LV endocardial chamber function (LVEF and eFS) were observed, but LV tissue mechanics improved following WL, evidenced by an increase in LVGLS (Table 3, Figure 3C).

CHANGES IN THE RV AND VENTRICULAR INTERACTION FOLLOWING WEIGHT LOSS. RV midcavity and longitudinal dimensions significantly decreased following surgery (Table 3). Analogous to changes in the LV, RVGLS and RVFWLS both improved following WL, without a significant change in RV fractional area change (Figure 3C). WL was not associated with changes in estimated RV systolic pressure or estimated right atrial pressure.

The reduction in EAT was coupled with significant decreases in measures of pericardial restraint and ventricular interdependence, including ideal/actual radius and LV eccentricity index (Table 3, Figure 3C). Although total heart volume did not change significantly, biventricular volume decreased and the ratio of biatrial volume/total heart volume increased.

CHANGES IN ESTIMATED LA PRESSURE, STRUCTURE, AND FUNCTION. Despite favorable changes in biventricular remodeling and systolic mechanics following surgical WL, at the median follow-up of 5.3 years, LA volume had increased, LA reservoir strain decreased, and LV filling pressures estimated by the E/e' ratio increased (Table 3). Time-dependent impairments in

TABLE 3 Longitudinal Changes in Left and Right Heart Structure and Function

	n	Examination 1	Examination 2	*P* Value Examination 1 vs 2	Change From Baseline
Left heart structure and function					
Septal wall thickness, mm	176	11.2 ± 1.9	10.8 ± 1.7	0.02	−0.4 ± 2.0
Posterior wall thickness, mm	176	10.8 ± 1.6	10.0 ± 1.5	<0.0001	−0.8 ± 1.8
LV end-diastolic dimension, mm	185	50.5 ± 5.7	50.4 ± 5.9	0.83	−0.1 ± −5.7
LV end-systolic dimension, mm	185	32.0 ± 4.8	32.5 ± 5.3	0.14	−0.7 ± 5.0
Relative wall thickness	173	0.43 ± 0.7	0.40 ± 0.07	<0.0001	−0.03 ± 0.09
LV end-diastolic volume, mL	185	123 ± 33	123 ± 34	0.85	0 ± 32
LV end-systolic volume, mL	185	42 ± 16	44 ± 19	0.10	2 ± 15
LV mass, g	173	206 (169-244)	181 (154-233)	0.0002	−16 (12-53)
LV mass/height$^{2.7}$(g/m$^{2.7}$)	173	49 (43-60)	46 (40-56)	0.003	−3 ± 13
LV ejection fraction, %	173	66 ± 7	64 ± 8	0.003	−2 ± 7
Endocardial fractional shortening, %	185	36.6 ± 4.9	35.2 ± 5.7	0.003	−1.4 ± 6.2
Cardiac output, mL/min	156	6.9 (5.9-7.8)	6.3 (5.2-7.2)	<0.0001	−0.6 ± 1.8
Stroke volume, mL	156	98 (83-113)	93 (78-107)	0.006	−6 ± 25
Left atrial volume, mL	150	61 (47-79)	69 (54-87)	<0.0001	8 ± 23
Mitral annular e', cm/s	173	8.1 ± 2.3	7.4 ± 2.4	0.002	−0.7 ± 2.7
E/e' ratio	171	10.0 (8.2-14.0)	11.3 (8.6-15.0)	0.04	0.9 (−2.0 to 3.2)
LVGLS, %	158	14.3 ± 3.2	15.1 ± 3.0	0.0006	0.8 ± 3.0
LV systolic dysfunction, %[a]	158	111 (71)	94 (59)	0.005	−17 (−12)
LA strain, %	137	26.6 ± 8.4	24.5 ± 8.8	0.002	−1.8 ± 10.1
Right heart structure and function					
RV basal dimension, mm	158	37.8 ± 7.0	37.8 ± 7.9	0.11	−1.0 ± 7.6
RV midcavity dimension, mm	157	32.3 ± 6.6	30.6 ± 6.5	0.02	−1.0 ± 8.1
RV longitudinal dimension, mm	157	78.3 ± 9.8	76.4 ± 8.7	0.006	−2.5 (−6.7 to 2.8)
RV fractional area change, %	142	41.6 ± 7.8	42.4 ± 8.5	0.31	−0.8 ± 9.9
Estimated RVSP, mm Hg	157	31.9 ± 10.5	32.4 ± 9.3	0.89	0.4 ± 11.2
Estimated RA pressure, mm Hg	163	6.1 ± 2.5	6.3 ± 3.2	0.66	0.1 ± 3.3
RVGLS, %	122	18.2 ± 4.8	19.5 ± 4.3	0.002	1.3 ± 6.2
RVFWLS, %	123	22.2 ± 5.8	24.2 ± 5.6	0.009	2.0 ± 8.1
RV systolic dysfunction, %[a]	123	42 (34)	24 (20)	0.02	−18 (−14)
Pericardial restraint					
EAT thickness, mm	179	7.4 ± 3.8	5.5 ± 3.5	<0.0001	−1.8 ± 3.7
Total heart volume, mL	167	865 (740-1,146)	853 (733-1,064)	0.10	−40 ± 254
Biatrial volume, mL	167	223 (183-316)	250 (189-334)	0.26	11 ± 112
Biventricular volume, mL	167	654 (541-819)	616 (531-754)	0.0007	−50 ± 184
Biatrial volume/total heart volume, %	167	36 (29-45)	39 (31-51)	0.0005	2.1 ± 6.8
Ideal/actual radius at end diastole	157	1.17 ± 0.12	1.12 ± 0.09	<0.0001	−0.04 ± 0.14
Ideal/actual radius at end systole	132	1.02 ± 0.09	0.99 ± 0.14	0.006	−0.05 ± 0.12
Eccentricity index at end diastole	157	1.10 ± 0.13	1.02 ± 0.11	<0.0001	−0.07 ± 0.15
Eccentricity index at end systole	133	1.13 ± 0.09	1.09 ± 0.08	<0.0001	−0.03 ± 0.11

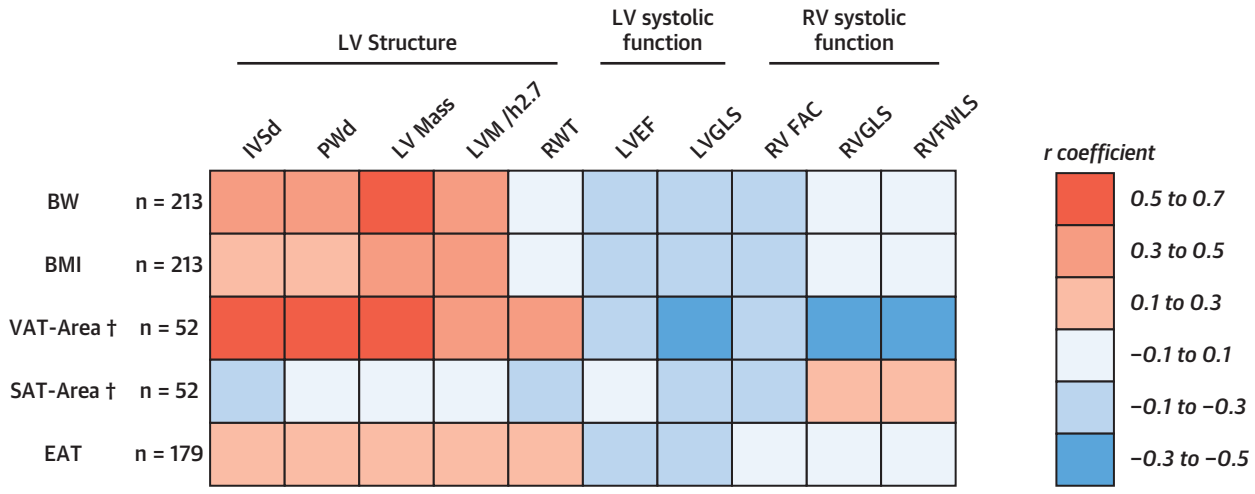
Values are mean ± SD, median (IQR), or n (%), unless otherwise indicated. [a]Normal value of left ventricular (LV) global longitudinal strain (GLS) is defined by LVGLS ≥16%, and that of right ventricular (RV) free wall longitudinal strain (FWLS) is defined as RVFWLS ≥20%.

EAT = epicardial adipose tissue; IVS = interventricular septal; LA = left atrial; PW = posterior wall; RA = right atrial; RVSP = right ventricular systolic pressure; RWT = relative wall thickness.

LA reservoir strain were similar in patients who did or did not develop atrial fibrillation between examinations.

Increases in LA volume were found to be greater in those with follow-up duration greater than the median (+11 ± 23 mL vs +4 ± 22 mL; $P = 0.049$), with similar findings observed for E/e′ (+1.5 [IQR: −1.7 to +3.9] vs −0.4 [IQR: −2.7 to +2.5]; $P = 0.04$) (Supplemental Figure 4), suggesting that part of the increase is related to time-dependent progression in LA myopathy associated with aging. In univariate linear regression analysis, there were significant associations between changes in LA volume ($\beta = 1.19$ [95% CI: 0.04-2.33]; $P = 0.04$); and E/e' ratio ($\beta = 0.25$ [95% CI: 0.01-0.50]; $P = 0.04$) with the duration between examinations, whereas other changes in

FIGURE 2 **Heatmap Showing Correlations Between Body Compositions and Cardiac Structure/Function**



Colors show strength and direction of correlation between measures of body fat with myocardial structure and function in the study cohort. †Available for n = 52. BMI = body mass index; BW = body weight; EAT = epicardial adipose tissue; EF = ejection fraction; FAC = fractional area change; FWLS = free wall longitudinal strain; GLS = global longitudinal strain; IVSd = interventricular septal dimension; LV = left ventricular; LVM = left ventricular mass; PWd = posterior wall dimension; RV = right ventricular; RVFWLS = right ventricular free wall longitudinal strain; RWT = relative wall thickness; SAT = subcutaneous adipose tissue; VAT = visceral adipose tissue.

cardiac structure/function were not related to the time interval between examinations (Supplemental Table 3), supporting this potential explanation.

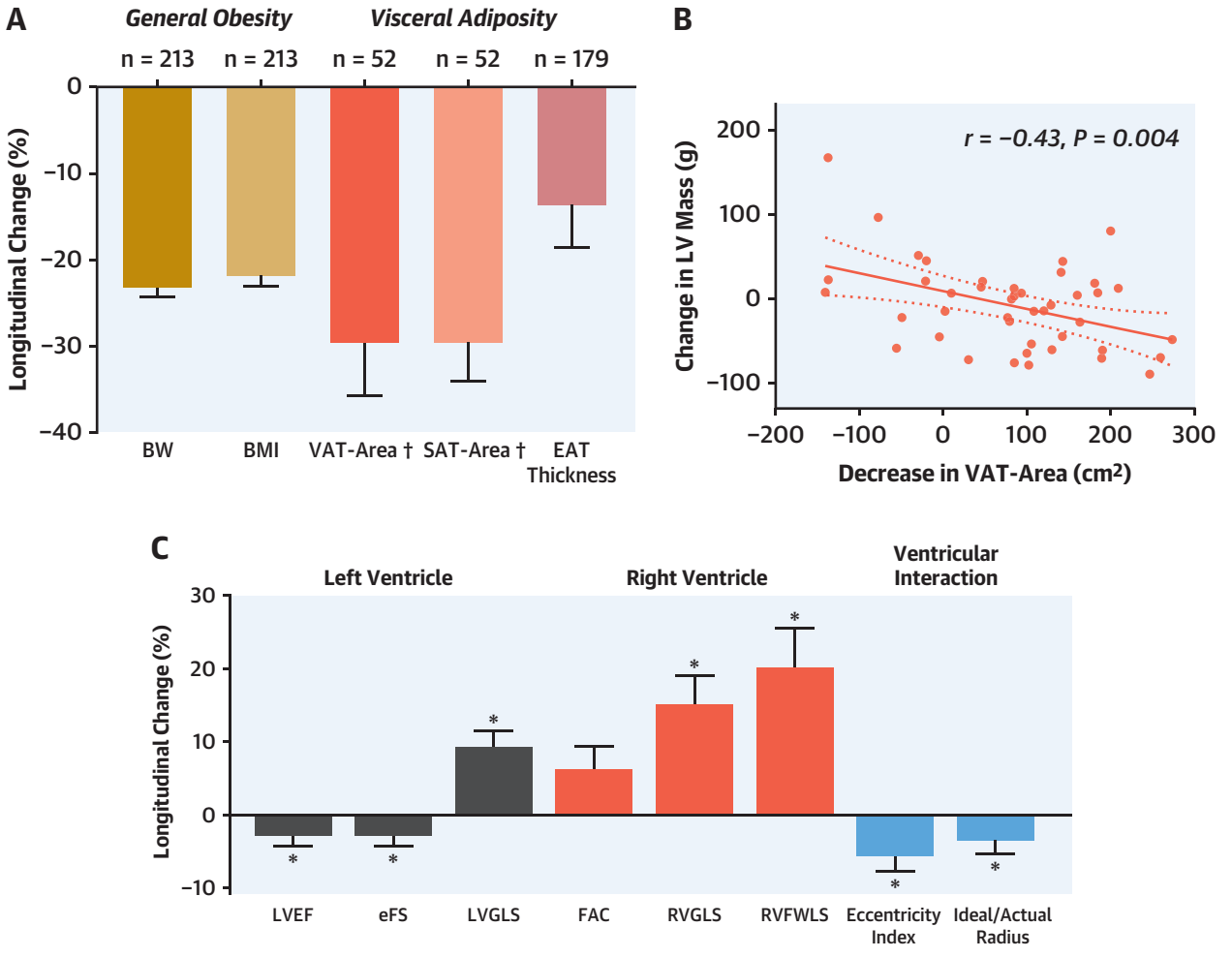
LA volume enlarged and E/e' increased more in patients with new-onset heart failure compared to those without (Supplemental Table 4), but there were no significant differences among those with new onset of atrial fibrillation (Supplemental Table 5).

DISCUSSION

In this study, we aimed to characterize the impact of bariatric surgery on fat distribution and changes in the heart in patients with medically complicated obesity over a longer-term follow-up than previously reported, with a focus on the relationships with visceral fat reduction in the abdomen and epicardial space (**Central Illustration**). In agreement with prior studies, LV reverse remodeling was observed following bariatric surgery in the entire population, and here we show that these changes were observed to be most strongly tied to reductions in visceral fat rather than subcutaneous fat or body weight in the smaller subgroup of patients with abdominal CT imaging. Favorable changes in ventricular structure were coupled with modest reduction in endocardial functional indexes, but improvements in LV and RV systolic mechanics, assessed by LVGLS, RVGLS, and RVFWLS. Decreases in LV mass and RV size were coupled with significant reductions in epicardial fat, leading to decreases in pericardial restraint and ventricular interaction. Despite favorable effects on biventricular remodeling and mechanics, there was progression in LA remodeling and worsening LA dysfunction, with increasing prevalence in atrial fibrillation, and greater elevation filling pressures, at least as estimated by E/e' ratio. These data suggest that although WL is beneficial for many of the cardiac changes that lead to HFpEF, the risk is not fully reduced over time, despite marked weight loss. These data underline the priority for randomized controlled trials testing the effects of WL on cardiac function and clinical outcomes in patients with or at risk for HFpEF.

VISCERAL FAT AND CARDIOVASCULAR STRUCTURE AND FUNCTION. In cross-sectional analyses, we observed that LV remodeling and dysfunction was more strongly correlated with visceral adiposity rather than subcutaneous fat, or with general obesity as measured by BW or BMI. Obesity, especially visceral adiposity, is recognized as a central player of cardiac dysfunction related to HF.[3,4] Visceral adipose secretes proinflammatory adipokines, leading to a chronic low-grade systemic inflammation,[19] as well as profibrotic mediators that may contribute to remodeling and diastolic dysfunction.[20] Excess visceral adipose may promote plasma volume expansion

FIGURE 3 Effects of Weight Loss on Cardiac Structure and Function



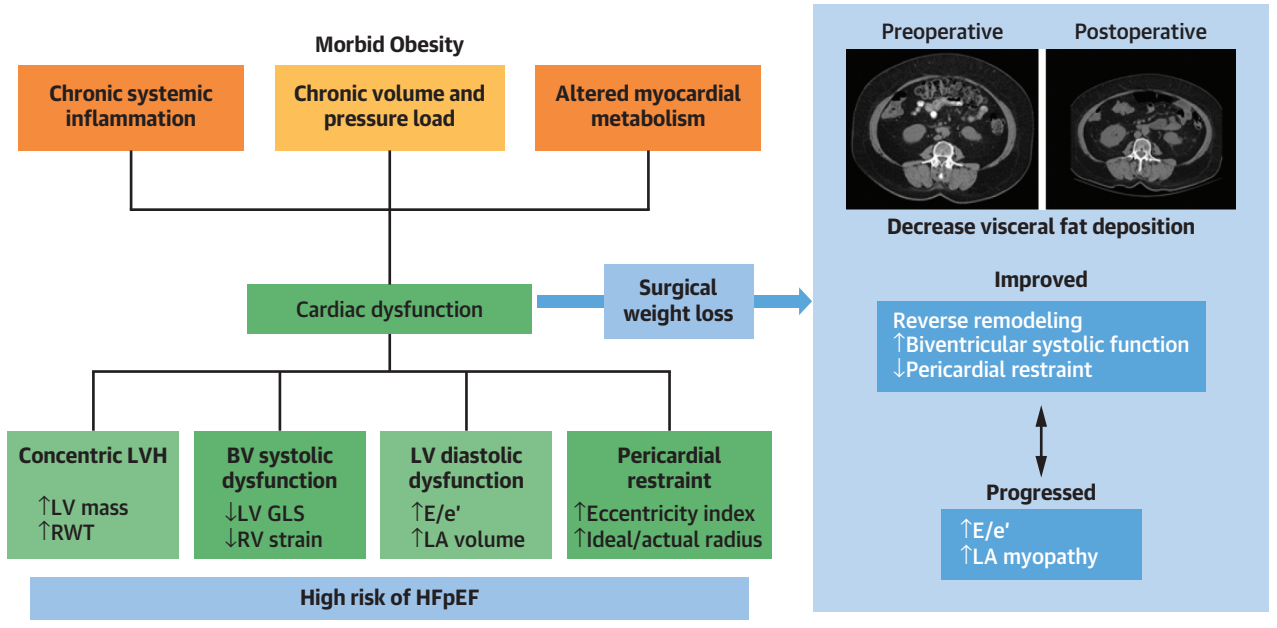
(A) Changes in body mass components. **(B)** Changes in LV mass were modestly correlated with changes in VAT area. **(C)** Reduction in LVEF and endocardial fractional shortening (eFS) and improvements in LV GLS were observed. RV FAC did not change, but RV GLS and RV FWLS improved. Ventricular interaction assessed by LV eccentricity index and ideal-to-actual LV ratio was reduced following surgical weight loss. Eccentricity index and Ideal/actual radius were measured at end diastole. *$P < 0.05$ between examinations 1 and 2. †Available for n = 52. **(A and C) Error bars** indicate SEM. **(B) Solid line** represents regression line and **dashed lines** represent 95% CI. EAT = epicardial adipose tissue; other abbreviations as in Figure 2.

through the activation of neurohormones.[21] The fact that LV wall thickness and RVGLS were more strongly correlated with VAT than BW or BMI supports a relatively stronger impact of visceral adiposity on cardiac dysfunction in morbid obesity, just as recently identified in HFpEF.[4]

We observed a 20% to 25% reduction in BW following bariatric surgery, but VAT area decreased (numerically) to a greater extent (by 30% reduction). Changes in LV mass were correlated with changes in VAT area (r = −0.43; $P = 0.004$) (Figure 3B) but not SAT area (r = 0.05; $P = 0.80$), again pointing to a more important role for visceral fat reduction in obesity-related heart disease. Further study is required to determine whether and how reductions in VAT might have a causal role in the observed changes in cardiac structure and function in obesity.

IMPROVEMENT IN LV MECHANICS FOLLOWING WEIGHT LOSS. In patients with preserved EF, WL has been associated with variable effects on LV systolic function measured at the endocardium, with results ranging from benefit, to no change, to slight impairment.[11,13] In the present study, we observed an

CENTRAL ILLUSTRATION **Cardiac Dysfunction in Obesity and Effect of Surgical Weight Loss**



Sorimachi H, et al. J Am Coll Cardiol. 2022;80(16):1501–1512.

Systemic inflammation, volume overload, and derangement of myocardial metabolism caused by morbid obesity result in myocardial dysfunction. Surgical weight loss improved left ventricular (LV) remodeling, biventricular function, and pericardial restraint. In contrast, elevation of E/e' and left atrial (LA) myopathy progressed. GLS = global longitudinal strain; HFpEF = heart failure with preserved ejection fraction; RV = right ventricular; RWT = relative wall thickness.

improvement in LVGLS in agreement with a few small series with shorter follow-up durations,[22-24] but this occurred despite modest reductions in endocardial function (LVEF and eFS).

Although the disagreement between effects on myocardial deformation (GLS) and endocardial function may seem perplexing or even concerning at first blush, this finding may be predictable based upon the confounding effects of LV remodeling on endocardial function. Stokke et al[25] demonstrated that increases in wall thickness allow for preservation of EF despite impairments in myocardial deformation, essentially concealing systolic dysfunction in such patients. This mirrors what is seen in HFpEF as well, where there are abnormalities in midwall myocardial shortening and GLS, despite normal EF, in relation to increases in concentric remodeling.[26,27]

The present results are consistent with this relationship in patients with obesity, most of whom did not have frank HFpEF, as it appears that the modest reductions in EF and eFS observed following surgery are related to reverse remodeling rather than an impairment in systolic function. This is consistent with findings from Owan et al,[10] who observed striking improvements in midwall fractional shortening 2 years following bariatric surgery, despite no change in EF. Midwall shortening is determined by the contraction of muscle fibers oriented in orthogonal directions at the inner and outer surfaces of the heart, and is thus highly sensitive to impairments in longitudinal systolic function, which are better reflected by GLS.[25,26]

IMPROVEMENT IN RV MECHANICS FOLLOWING WEIGHT LOSS. RV dysfunction is associated with poor prognosis in patients with HFpEF,[28,29] and patients with obesity-related HFpEF display more severe RV remodeling and dysfunction compared with nonobese patients.[6] Mirroring the LV, RV strain correlated negatively with VAT area but did not correlate with BW or BMI (**Figure 1**), and both RVGLS and RVFWLS improved after bariatric surgery (**Figure 3C**). These findings suggest that WL, particularly reduction in visceral adiposity, benefits RV structure and function in a manner akin to that observed in the LV. One pertinent neutral finding

relates to the absence of an effect on RV afterload, estimated by RVSP, which did not change following WL. This finding disagrees with a prior meta-analysis of invasive studies.[30] The reason for the discrepancy is not clear, but may relate to the use of echocardiography to estimate hemodynamics, as recent data indicate that relationships between echocardiographic hemodynamic estimates and directly measured values differ between patients with and without excess body fat.[31]

The mechanism of benefit for LV and RV systolic mechanics following WL cannot be determined from the present study, but obesity is known to increase myocardial oxygen demand and impair efficiency,[32] and prior studies have shown improvements in myocardial metabolism and energy utilization following WL, which may contribute.[7] Favorable changes in blood pressure and plasma volume may certainly contribute. Obesity is also associated with myocardial steatosis, which has been correlated with impairments in GLS in patients with diabetes but no HF[33] and may be reduced through long-term WL.[34]

REDUCTIONS IN EPICARDIAL FAT AND VENTRICULAR INTERACTION. Patients with HFpEF and increased EAT display greater elevation in cardiac filling pressures, more severe pulmonary hypertension, amplified pericardial restraint, poorer exercise capacity, and as recently shown, increased risk for adverse outcomes.[6,16,35-37] Increases in EAT have also been strongly tied to abnormalities in myocardial deformation and fibrosis in patients without HF.[38,39] Excessive EAT has been proposed as a potential source of inflammatory adipokines that may influence myocardial function and contribute to HFpEF.[40]

The present study revealed a decrease in EAT, mirroring changes in abdominal VAT. The reduction in EAT following bariatric surgery was proportionately less than abdominal VAT, in agreement with an earlier study,[41] but the pathophysiological significance for even minor reductions in EAT may be substantial for several reasons. In addition to soluble effects related to adipokines, increases in EAT and epicardial heart volume amplify coupling between the right and left sides of the heart, a phenomenon known as ventricular interdependence.[6,42] Here, we show for the first time that WL induced through bariatric surgery may reduce this pericardial restraint and ventricular interdependence, which would be expected to reduce cardiac filling pressures and relieve lung congestion.[31,42]

The observed increase in E/e' over time was surprising in light of prior invasive studies showing favorable reductions in directly measured cardiac filling pressures following WL.[30] However, it may be that E/e' is not a reliable estimate of LV filling pressures in this setting, or that its relationship with directly measured LA pressure differs with body mass.[31] Indeed, an increase in extrinsic restraint on the heart (as with increased EAT) reduces the transmural distending pressure relative to measured intracavitary pressure. Surgical WL may shift in this relationship, such that a higher E/e' is actually reflective of the same or even lower filling pressure.[31]

UNCOUPLING OF ATRIAL AND VENTRICULAR EFFECTS. Despite improvements in ventricular remodeling, function, and pericardial restraint following WL, LA structure and function deteriorated, with an increase in LA volume, decrease in LA reservoir strain, elevation in estimated LA pressures, and increase in the prevalence of AF. In obese patients, LA volume is positively related to LV mass,[43] suggesting that WL should reduce LA volume; however, here we show that LA enlargement progresses in obesity-related heart disease over longer durations of follow-up, despite beneficial reverse LV remodeling that occurs early and is maintained. This may partly reflect the effects of time, because prior studies in community-based samples indicate that LA volume and E/e' ratio both increase as part of normal aging,[44] but the disconnect between atrial and ventricular effects is nonetheless notable and suggests a fundamental difference. A recent meta-analysis of observational studies demonstrated a highly significant 50% reduction in the incidence of new-onset HF following bariatric surgery, but there was no significant effect on incident AF.[9] The present results revealing progression of LA myopathy, despite favorable effects at the ventricle level, may help explain this relatively less marked improvement in AF reduction following WL. However, these results are difficult to interpret because of the lack of a control group of patients who did not undergo WL surgery. This further points to the importance of prospective trials.

STUDY LIMITATIONS. This is a retrospective observational study and is restricted to patients referred for and who underwent bariatric surgery, all of which introduces bias. There was no separate control group of patients with obesity but no WL intervention, precluding the ability to make inferences regarding causality. Multiple metabolic, physical, and loading changes occur following bariatric surgery, including improvements in insulin sensitivity, reductions in blood pressure and lipids, and decrease in obesity-related comorbidities such as sleep apnea;

the present analysis cannot determine the extent to which observed changes in cardiac structure and function were related to WL alone or to these coexisting changes. These limitations emphasize the importance of performing rigorous randomized controlled trials testing WL through surgical, lifestyle, or pharmacological interventions. Some such trials are already underway, evaluating the effects of pharmacological WL induced by GLP-1 receptor agonists and combined GLP-1/GIP agonists (NCT04788511, NCT04847557) on clinical endpoints such as quality of life and physical function. The retrospective nature of the study restricts the sample to patients who underwent necessary imaging, leading to selection bias. In addition, the important variables supporting the associations of cardiac structure and function with visceral adiposity were derived from a smaller subgroup including 25% of patients. Although this data missingness could create bias, baseline characteristics were similar in the subgroup with VAT data (Supplemental Table 2), overall relationships between body weight and cardiac structure/function were similar to the broader sample (Supplemental Figures 2 and 3), and it seems less likely a priori that referral for abdominal imaging would influence the relationship between VAT or VAT changes and cardiac structure/function.

CONCLUSIONS

In this observational study, weight loss following bariatric surgery was observed to be associated with LV reverse remodeling, improved longitudinal biventricular mechanics, and reduced ventricular interaction, and these benefits seemed to be related to reductions in abdominal and epicardial visceral fat after long-term follow-up. Despite beneficial effects in the ventricles, LA structure and function deteriorated over time, which may contribute to the less-marked reduction in AF noted following bariatric surgery. These data provide new insights into the effect of WL on cardiac dysfunction in obesity-related heart disease and emphasize the priority for future controlled trials testing the effects of surgical, pharmacological, and lifestyle WL interventions on the heart and clinical outcomes in patients with or at risk for obesity-related HFpEF.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Weight loss following bariatric surgery is associated with improvement in ventricular structure and function, loss of visceral and epicardial fat, and reduction in ventricular interdependence.

TRANSLATIONAL OUTLOOK: Prospective trials are needed to evaluate the effect of surgically induced weight loss in patients with obesity-related HFpEF.

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KEY WORDS bariatric surgery, cardiac function, cardiac structure, heart failure, obesity

APPENDIX For an expanded Methods section as well as supplemental figures and tables, please see the online version of this paper.