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Effects of Bariatric Surgery on Early Myocardial Alterations in Adult Severely Obese Subjects

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Key Words

Bariatric surgery · Color Doppler myocardial imaging · Insulin resistance · Integrated backscatter · Myocardial dysfunction · Obesity · Strain · Strain rate

Abstract

Objective: Aim of this study was to investigate the effect of weight loss on structural and functional myocardial alterations in severely obese subjects treated with bariatric surgery. ***Patients and Methods:*** Thirteen severely obese patients (2 males and 11 females) were enrolled in the study. All subjects underwent conventional 2D color Doppler echocardiography. The new ultrasonic techniques used were: (a) integrated backscatter for the analysis of myocardial reflectivity, referred to pericardial interface as expression of myocardial structure (increase in collagen content) and of cyclic variation index as expression of intrinsic myocardial contractility and (b) color Doppler myocardial imaging (CDMI) for the analysis of strain and strain rate (myocardial deformability). All subjects underwent bariatric surgery and were re-submitted to echocardiographic and biochemical examination 6–24 months after surgery. ***Results:*** The main finding of the present study was a quite complete normalization of myocardial functional and structural alterations after weight loss. In particular, the cyclic variation index at septum level improved from 14.6 ± 7.0 before to 25.7 ± 11.2 (means ± SD) after surgery (controls: 36.2 ± 9.1). Mean reflectivity at septum level significantly decreased from 55.8 ± 9.5 to 46.5 ± 8.8 (controls: 43.0 ± 8.0). Also, the strain at septum level significantly improved after surgery (from –11.9 ± 3.2 to –20.4 ± 5.3; controls: –23.4 ± 9). ***Conclusion:*** This study establishes: (a) the utility of new ultrasonic techniques to detect very early structural and functional myocardial alterations in severely obese patients, and (b) the regression of these subclinical abnormalities after weight loss achieved by bariatric surgery.

Introduction

Obesity is a chronic medical problem with dramatically rising trends in its worldwide prevalence, to an extent that is now recognized as a global epidemic [1]. The risk of a premature death is higher in obese than non-obese indi-

[1] Project for the technologic innovation in the diagnosis and prognosis of cardiovascular diseases (Dir. Prof. M. Mariani).

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viduals, and the risk of death by cardiovascular disease is five times increased [2–4].

Obesity is a well-established risk factor for congestive heart failure, being frequently associated with type 2 diabetes, hypertension and dyslipidemia [5]. Recent studies suggest that insulin resistance may be the mediator between obesity and congestive heart failure [6–8]. A variety of adaptations/alterations in cardiac structure and function have been detected in patients with morbid obesity, and peculiar pathogenic mechanisms, e.g. cardiac steatosis, lipoapoptosis and the activation of specific cardiac genes, have been described [9, 10]. Using very sensitive intramyocardial ultrasonic techniques, early myocardial structural and functional alterations have been observed in obese subjects [11–14], suggesting the existence of an 'obese cardiomyopathy' as the complex combination of the effects of both hemodynamic and metabolic alterations.

Bariatric surgery represents an effective alternative for the treatment of obesity when non-surgical weight loss programs (diet + behavior modification + regular exercise) have failed [15, 16]. The aim of this study was to analyze the effect of weight loss achieved by bariatric surgery on the early subclinical myocardial alterations detected in a group of severely obese adult subjects using both integrated backscatter (IBS) and color Doppler myocardial imaging (CDMI). All subjects were examined before and 6–24 months after treatment with the Roux-en-Y gastric bypass.

Patients and Methods

Study Population

Thirteen consecutive patients with severe obesity (2 males and 11 females) presenting to our Obesity Center for the diagnosis and cure of their weight problems were enrolled in the study after informed consent was obtained (table 1). Clinical, hematological and instrumental examinations were performed following the Italian guidelines for obesity [17] and each patient was treated according to appropriate protocols for his/her condition. Anthropometric measurements were performed after an overnight fast. Body weight was measured to the nearest kilogram and body height to the nearest centimeter. Exclusion criteria were impairment in left ventricular systolic function (ejection fraction <40%), congestive heart failure, significant valvular heart disease by Doppler analysis and cardiomyopathy. All obese patients had a negative history of myocardial infarction or coronary artery disease. Once selected, all participants underwent echocardiography, thus reserving eligibility for the study to those with a good acoustic window. All patients underwent bariatric surgery without complications and were reevaluated after 6–24 months using the same ultrasonic protocol of investigation. Thirteen age- and sex-matched non-obese healthy subjects were recruited as controls.

Experimental Procedure

Biochemistry. Blood samples were taken for biochemical analysis of renal function, electrolytes, fasting insulin and glucose, total cholesterol and triglycerides, LDL and HDL cholesterol.

Assessment of Insulin Resistance. Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated as fasting glucose (in mM) × fasting insulin (in mU/ml)/22.5 [18]. Estimates of HOMA-IR correlate well with euglycemic clamp data.

Echocardiographic Analysis

Conventional 2D Doppler Echocardiography. Conventional echocardiographic studies were performed with a digitized Philips Sonos 7500 echograph equipped with a broadband sector transducer (S3 fusion imaging), as previously described [19].

Pulsed-Wave Tissue Doppler Imaging (PW-TDI). In the apical four chamber view, pulsed-wave Doppler sample volume was subsequently placed in two different regions of the mitral annulus: septal and lateral [14, 20]. The detailed method has been described previously. PW-TDI of the septal annulus was used to measure early peak diastolic mitral annulus velocity (E_s). Left ventricular filling pressures were estimated by the relationship of E/E_s (E being derived by mitral flow velocity).

CDMI-Derived Indices: Mean Regional Velocities, Strain Rate and Strain. CDMI data, digitally recorded with a Philips Sonos 7500 echograph, were analyzed offline using dedicated software (AMID, Italy). A myocardial segment contained inside a region of interest was considered entirely. Frame rate ranged between 75 and 100 Hz. Velocity, strain (ε) and strain rate profiles [21] were averaged over three consecutive cardiac cycles to derive mean velocity and strain rate curves over a mean RR interval. Strain is defined as the deformation of an object, normalized to its original shape and strain rate is the speed at which deformation (i.e. strain) occurs (its unit is s^{-1}). To describe deformation in longitudinal direction both at the medium posterior septum and the medium lateral wall, the following parameters were calculated in apical chamber view in all study subjects: maximum strain (ε_{sys}) in percent; maximum strain rate (SR_{sys}) per second and early (SR_E) and late diastolic peak strain rate (SR_A) in centimeters per second.

The intraclass correlation coefficient (r_i) was calculated according to Bland and Altman's procedure [21]. Almost three values of strain rate and strain were sampled for each patient and for each segment: septal and lateral; the correlation coefficient (r_i) was 0.86 for septal and 0.89 for lateral segments.

Acoustic Densitometry. Commercial high frame rate IBS technology has been applied to provide a more robust signal (calibrated in dB) with a substantial improvement in the time sequence of backscattered signals, further optimized for tissue characterization research. The images were obtained using a harmonic imaging mode. A detailed IBS methodology has been described previously [22, 23].

Statistical Analysis

Continuous variables were expressed as means ± SD. Analysis of variance for the three study groups was also performed with a Tukey test to analyze significant differences between parameter means obtained by intragroup comparisons of the obese patients (both before and after bariatric surgery) and between both obese groups and controls. Upper and lower 95% confidence limits for each variable were calculated from the 2-tailed Student's t test dis-

Table 1. Demographic and clinical findings

Parameters	Obese patients		Controls (n = 13)	p value
	before surgery (n = 13)	after surgery (n = 13)		
Age, years	31.2 ± 6.1	–	33.2 ± 6.4	NS
Height, cm	166.3 ± 7.3[d]	–	172.6 ± 7.4	<0.001
Weight, kg	126.4 ± 20.3[d]	93.6 ± 16.3[b, e]	74.8 ± 8.2	<0.001
Body surface, m^2	2.19 ± 0.3[d]	1.88 ± 0.2[a, e]	1.85 ± 0.2	<0.001
BMI, kg/m^2	47.0 ± 8.1[d]	36.0 ± 5.0[b, e]	22.8 ± 2.8	<0.001
SAP, mm Hg	128.2 ± 13.7	120.6 ± 8.5	120.2 ± 4.3	NS
DAP, mm Hg	77.6 ± 9.3	77.9 ± 8.4	73.6 ± 6.5	NS
MAP, mm Hg	97.4 ± 4.8[c]	92.7 ± 4.5	85.4 ± 7.6	<0.05
HR, b/min	81.5 ± 8.7[d]	67.7 ± 8.2[a]	69.9 ± 11.2	<0.001
SV, ml	76.7 ± 7.4[c]	73.6 ± 6.8[a]	68.7 ± 8.7	<0.05
CO, l/min	5.8 ± 1.7[c]	5.3 ± 1.5[a, e]	5.02 ± 1.3	<0.05
Glycemia, mg/dl	93.8 ± 7.3[a, c]	81.2 ± 6.8	80.8 ± 7.5	<0.05
Total cholesterol, mg/dl	218.2 ± 15.3[a, c]	198.5 ± 10.2	176.3 ± 9.8	<0.05
HDL cholesterol, mg/dl	50.5 ± 9.2	53.9 ± 8.2	58.6 ± 8.3	NS
LDL cholesterol, mg/dl	134.2 ± 9.2	130.6 ± 7.6	133.5 ± 10.5	NS
Insulin	16.3 ± 8.6[d]	5.6 ± 6.2[b, e]	4.2 ± 2.1	<0.001
HOMA-IR	3.79 ± 1.6[d]	1.5 ± 0.7[a, e]	0.92 ± 0.5	<0.001

BMI = Body mass index; CO = cardiac output; DAP = diastolic arterial pressure; HR = heart rate; MAP = mean arterial pressure; NS = nonsignificant; SAP = systolic arterial pressure; SV = stroke volume. [a] $p < 0.05$, [b] $p < 0.01$, comparison between obese groups; [c] $p < 0.05$; [d] $p < 0.01$, comparison between obese patients before surgery and controls; [e] $p < 0.05$, comparison between obese patients after surgery and controls.

tribution using the following formulas: mean ± (2.042 × SD), and mean –(2.042 × SD), respectively. McNemar's test was also applied to statistically compare the methods employed: mitral flow pulsed Doppler and new ultrasonic technologies. The intraclass correlation coefficient (r_i) was calculated according to Bland and Altman's procedure [21], using one-way analysis of variance for repeated measurements. A p value <0.05 was considered significant.

Results

Anthropometric and clinical findings of the obese subjects and the controls are shown in table 1. Weight loss, expressed as a reduction in the body mass index, was 27.4 ± 14.7% (mean ± SD). A significant improvement in most study parameters was also observed.

After bariatric surgery, the main findings of conventional echocardiographic parameters were: a significant reduction in left atrial dimensions ($p < 0.0001$; table 2); a significant reduction in the septum and posterior wall thickness ($p < 0.001$); a significant reduction in both left ventricular mass (LVM) indexed by height (LVM_h; –23 ± 10%) and by body surface (LVM_{bs}; $p < 0.0001$ and $p < 0.05$, respectively) and a slight but significant reduction in left ventricular enddiastolic volume ($p < 0.05$; table 2).

The main findings of Doppler transmitral flow parameters were: a significantly lower peak A velocity and a lower isovolumic relaxation time in the obese group after surgery ($p < 0.01$) with a higher E/A ratio ($p < 0.01$; table 3).

The main findings of PW-TDI velocities and times at mitral annular level were: a significantly higher PW-TDI peak E annular velocity (septal) and a significantly lower peak A annular velocity (septal; $p < 0.001$); a significantly higher E/A ratio ($p < 0.001$); a significantly lower isovolumic relaxation time (septal; $p < 0.001$), a significantly higher systolic peak 'S' wave of annular motion (lateral; $p < 0.01$) and a significantly lower E/E_s (lateral) in the obese patients after surgery ($p < 0.0001$; table 4).

The main findings of CDMI parameters were: the increase and normalization of myocardial systolic strain (septal; mean Δ: +65 ± 35%) and of systolic strain rate (mean Δ: +62 ± 34%) in obese patients after surgery ($p < 0.001$ and $p < 0.003$, respectively; table 5).

Table 2. Conventional echocardiographic parameters

Parameters	Obese patients		Controls (n = 13)	p value
	before surgery (n = 13)	after surgery (n = 13)		
Aortic root, mm	31.7 ± 3.1	30.9 ± 2.7	31.9 ± 2.6	NS
Left atrium, mm	37.9 ± 3.9[d]	33.5 ± 4.6[a]	33.1 ± 3.7	<0.0001
EDD, cm	5.3 ± 4.3	47.7 ± 4.0	47.4 ± 3.8	NS
FS, %	39.3 ± 8.8	41.3 ± 5.6	35.8 ± 7.3	NS
EF, %	72.5 ± 9.9[c]	70.6 ± 8.8[e]	66.3 ± 8.6	<0.03
DS_{th}, mm	11.3 ± 1.9[d]	8.6 ± 1.6[b]	8.5 ± 1.2	<0.001
DPW_{th}, mm	9.9 ± 1.5[d]	8.2 ± 1.6[b]	8.5 ± 2.1	<0.001
LVM_h, g/m^2	56.2 ± 12.2[d]	41.8 ± 10.7[b]	37.1 ± 7.8	<0.0001
LVM_{bs}, g/m^2	94.5 ± 23.9	80.6 ± 19.8[a]	91.1 ± 18.4	<0.05
EDV, cm^3	85.2 ± 9.4[c]	65.3 ± 13.7[b]	75.8 ± 5.8	<0.05
ESV, cm^3	24.5 ± 9.2	23.8 ± 7.8[a]	28.5 ± 8.6	NS

DPW_{th} = Diastolic posterior wall thickness; DS_{th} = diastolic interventricular septum thickness; EDD = enddiastolic pressure; EDV = enddiastolic volume; EF = ejection fraction; ESV = endsystolic volume; FS = fractional shortening. [a] $p < 0.05$, [b] $p < 0.01$, vs. obese patients before surgery; [c] $p < 0.05$, [d] $p < 0.01$, obese patients before surgery vs. controls; [e] $p < 0.05$, obese patients after surgery vs. controls.

Table 3. Doppler transmitral flow parameters: velocities and times

Parameters	Obese patients		Controls (n = 13)	p value
	before surgery (n = 13)	after surgery (n = 13)		
Peak E, cm/s	84.8 ± 19.1	80.0 ± 18.9	80.2 ± 14.5	NS
Peak A, cm/s	75.1 ± 13.7[d]	64.5 ± 10.5[b]	53.7 ± 15.3	0.01
E/A ratio	1.18 ± 0.4[d]	1.3 ± 0.4[a]	1.4 ± 0.5	0.01
Mitral DT, ms	177.2 ± 32.5[d]	171.7 ± 23.9[a, e]	155.5 ± 31.9	0.01
IVRT, ms	80.2 ± 16.2[c]	71.8 ± 9.6[b]	77.8 ± 16.8	0.05

DT = Deceleration time; IVRT = isovolumic relaxation time. [a] $p < 0.05$, [b] $p < 0.01$, vs. obese patients before surgery; [c] $p < 0.05$, [d] $p < 0.01$, obese patients before surgery vs. controls; [e] $p < 0.05$, obese patients after surgery vs. controls.

The main findings concerning IBS parameters were: a significantly higher cyclic variation index, both at septum and at posterior wall level, in obese patients after surgery (mean septum Δ: 43 ± 25%, $p < 0.0001$, and mean posterior wall Δ: 28 ± 18%, $p < 0.001$); a slight but significant reduction in IBS_m, both at septum and at posterior wall level, in the obese group after surgery (mean septum Δ: –24 ± 10%, $p < 0.04$, and mean posterior wall Δ: –22 ± 10%, $p < 0.01$; table 6).

For all significant differences, a trend toward normalization was observed, with the majority of postsurgical obese parameters being comparable with those of the controls (tables 1–6).

Discussion

The recent American Heart Association scientific statement on obesity and cardiovascular disease [2] underlines that extreme obesity (class III) is associated with an extremely high risk for developing type 2 diabetes, hypertension and cardiovascular disease. The reading of this statement has prompted our present preliminary study, although the strictly homogeneous group of severely obese young patients analyzed before and after bariatric surgery was small.

In a prospective study, our group has recently demonstrated that severely obese patients presented, in the early

Table 4. PW-TDI findings in the study groups

Parameters	Obese patients		Controls (n = 13)	p value
	before surgery (n = 13)	after surgergy (n = 13)		
Septal				
PW-TDI S	7.8 ± 1.6	8.3 ± 0.9	8.6 ± 1.6	NS
PW-TDI peak E	7.8 ± 2.9[d]	8.7 ± 2.5	12.3 ± 2.3	<0.001
PW-TDI peak A	9.9 ± 2.1[d]	7.8 ± 2.2[b]	6.5 ± 1.9	<0.001
PW-TDI E/A	0.81 ± 0.7[d]	1.2 ± 0.6[b]	1.5 ± 0.6	<0.001
PW-TDI IVRT	73.4 ± 11.7[d]	67.8 ± 14.2[b]	75.4 ± 14.3	<0.001
Lateral				
PW-TDI S	7.7 ± 1.7[c]	10.0 ± 1.8[a]	11.2 ± 2.1	<0.01
PW-TDI peak E	11.5 ± 3.4[d]	14.7 ± 4.8	16.7 ± 4.1	<0.0001
PW-TDI peak A	10.8 ± 2.7[d]	8.8 ± 1.9	8.3 ± 2.7	<0.01
PW-TDI E/A	1.2 ± 0.4[d]	1.7 ± 0.3	2.1 ± 0.5	<0.002
PW-TDI IVRT	78.4 ± 19.8	59.5 ± 18.2[a]	72.6 ± 17.8	<0.05
E/E_s	12.8 ± 1.9[d]	7.8 ± 2.2[b, e]	6.6 ± 1.6	<0.0001

E_s = Early peak diastolic mitral annulus velocity; IVRT = isovolumic relaxation time; S = systolic peak S wave of annular motion. [a] $p < 0.05$, [b] $p < 0.01$, vs. obese patients before surgery; [c] $p < 0.05$, [d] $p < 0.01$, obese patients before surgery vs. controls; [e] $p < 0.05$, obese patients after surgery vs. controls.

Table 5. CDMI parameters (regional velocities, strain and stain rate)

Parameters	Obese patients		Controls (n = 13)	p value
	before surgery (n = 13)	after surgery (n = 13)		
Medium posterior septum				
ε_{sys}, %	–11.9 ± 3.2[d]	–20.4 ± 5.3[b]	–23.4 ± 9.4	<0.001
SR_{sys}, s^{-1}	–0.5 ± 0.2[d]	–1.1 ± 0.3[b]	–1.2 ± 0.4	<0.003
SR_E, cm/s	0.8 ± 0.4[d]	1.2 ± 0.2[a]	1.4 ± 0.6	<0.001
SR_A, cm/s	0.8 ± 0.3	0.5 ± 0.3	0.5 ± 0.4	NS
Medium lateral wall				
ε_{sys}, %	–10.5 ± 3.7[d]	–19.5 ± 4.7[b]	–21.4 ± 5.6	<0.0001
SR_{sys}, s^{-1}	–0.6 ± 0.3[d]	–1.2 ± 0.3[b, e]	–1.7 ± 1.7	<0.0001
SR_E, cm/s	1.1 ± 0.4[d]	1.3 ± 0.6[a]	1.3 ± 0.5	<0.001
SR_A, cm/s	0.6 ± 0.3	0.5 ± 0.2	0.5 ± 0.2	NS

ε_{sys} = Maximum strain; NS = nonsignificant; SR = strain rate; SR_A = late diastolic peak strain rate; SR_E = early diastolic peak strain rate; SRsys = maximum strain rate. [a] $p < 0.05$, [b] $p < 0.01$, vs. obese patients before surgery; [c] $p < 0.05$, [d] $p < 0.01$, obese patients before surgery vs. controls; [e] $p < 0.05$, obese patients after surgery vs. controls.

phase of their disease, some new systolic and diastolic subclinical functional abnormalities by ultrasonic IBS and CDMI (strain and strain rate), hypothesizing the existence of an 'obese cardiomyopathy'. These new findings, representing the very early markers of myocardial dysfunction, could predict which obese individuals are at highest risk of heart failure. The main finding of the present study was the quite complete normalization of left ventricular myocardial functional and structural alterations, evidenced by IBS and CDMI, in severely obese patients after bariatric

Table 6. IBS parameters

Parameters	Obese patients		Controls (n = 13)	p value
	before surgery (n = 13)	after surgery (n = 13)		
IBS p, dB	47.1 ± 5.6	47.5 ± 5.5	48.2 ± 4.9	NS
CVI_S, %	14.6 ± 7.0[d]	25.7 ± 11.2[b]	36.2 ± 9.1	<0.0001
CVI_{PW}, %	30.7 ± 6.7[d]	35.6 ± 9.5[b]	42.0 ± 8.6	<0.001
IBS_{MSI}, %	55.8 ± 9.5[c]	46.5 ± 8.8[a, e]	43.0 ± 8.0	<0.04
IBS_{MPWI},%	34.6 ± 5.9[d]	27.7 ± 7.4[a, e]	33.7 ± 7.1	<0.01

CVI_S/CVI_{PW} = Cyclic variation index at septum/posterior wall level; IBS_{MSI}/IBS_{MPWI} = mean septum/mean posterior wall IBS; NS = nonsignificant. [a] $p < 0.05$, [b] $p < 0.01$, vs. obese patients before surgery; [c] $p < 0.05$; [d] $p < 0.01$, obese patients before surgery vs. controls; [e] $p < 0.05$, obese patients after surgery vs. controls.

surgery. On the other hand, a similar trend was found between HOMA-IR and both LVM and mean septum reflectivity variations, to express normalization of insulin resistance and regression of left ventricular hypertrophy (LVH) with normalization of its collagen content.

Hemodynamic and Metabolic Repercussion of Obesity

Obesity induces several modifications in cardiac structure and function, which are associated with hemodynamic overload [11–13, 24, 25] and represents itself a risk factor for congestive heart failure [5, 26–28]. Atrial and ventricular remodeling is common in obese patients, and it is known that these physiopathological aspects are related to atrial and ventricular dysfunctions. The larger atrial size in obese patients is related both to an expanded intravascular volume and to altered left ventricular filling. In particular, in normotensive obese patients, eccentric LVH represents an adaptation to the expanded intravascular volume. In addition to the increased preload, left ventricular afterload is elevated due to both higher vascular resistance caused by excess adipose tissue and greater conduit artery stiffness. Body mass index is related to impaired diastolic functional indices; obesity can alter diastolic filling parameters because of altered load conditions, as well as due to increased LVM_h.

LVH determines impaired left ventricular diastolic function, essentially in the late diastolic passive phase, linked to increased myocardial stiffness; this alteration is considered an early event of cardiac involvement in obese subjects followed by impaired systolic function. Systolic parameters (ejection fraction and fractional shortening) are normal or supernormal in obese patients compared with controls.

Left ventricular diastolic function, evidenced by the E/A ratio conventionally obtained by transmitral flow Doppler analysis, is significantly reduced in obese patients, essentially due to a significantly higher peak A.

PW-TDI parameters, sampled at mitral annular level, which are the expression of global left ventricular longitudinal function, showed that all intramyocardial diastolic phases are altered in severe obesity. The significantly lower mitral annulus early diastolic velocity (E_s and El) and the significantly higher E/E_s and E/El ratios, directly related to left ventricular filling pressure [19], are further evidence of the presence of a left ventricular diastolic dysfunction in obesity.

The use of intramyocardial ultrasonic techniques (e.g. IBS and CDMI) allowed us to detect minimal, very early alterations in systolic and diastolic phases in the obese [12, 13]. In particular, backscatter showed a higher level of myocardial echoreflectivity in the septum and structural myocardial alterations (increased myocardial fibrosis) in severe obese patients [23] (moderate and severe myocardial fibrosis is a frequent autopsy finding in obese patients [29]). Despite the lower cyclic variation index, both at septum and posterior wall level, expression of an early impairment in intrinsic myocardial contractility was also detected in obese patients when left ventricular ejection fraction was above normal.

Systolic deformation (evidenced by strain and strain rate) appears significantly impaired in the obese before surgery, representing an early myocardial functional abnormality, which can occur concomitantly with diastolic dysfunction, even if the common conventional echocardiographic functional parameters are within the normal range.

Impact of Weight Loss on Cardiac Structure and Function

Weight loss has beneficial effects on functional and structural cardiac alterations; in particular in previous studies LVM was altered by weight loss. In obese patients subjected to bariatric surgery, a significant reduction in LVM was observed using electrocardiographic criteria of LVH and echocardiographic criteria (reduced LVM with significant reductions in the thickness of both septum and posterior wall of left ventricle). Weight loss decreases oxygen consumption at any given work rate, cardiac output, blood pressure and filling pressures of left ventricle as stroke volume diminishes [30].

Regarding structural aspects, bariatric surgery resulted in a significant reduction in LVM, essentially caused by a significant reduction in septum and posterior wall thickness and by a reduction in enddiastolic volume. A significant reduction in interstitial collagen content was shown by the significant reduction in ultrasonic reflectivity (IBS_{MS}) after surgery. The reduction in left atrial dimension in the obese group after surgery is the expression of a reduced preload, confirmed by the reduction in enddiastolic volume. The better left ventricular load conditions induced by weight loss were furthermore confirmed by the significant reduction in the E/E_s ratio in the obese group after surgery, which represents an index of the enddiastolic left ventricular pressure level.

Weight loss after bariatric surgery in severely obese patients caused improvements in left ventricular systolic and diastolic functions. In particular, an increase in myocardial deformability (postsurgical systolic strain and strain rate) and an improvement in myocardial intrinsic contractility (cyclic variation index at septum and posterior wall level) was noted. The significant improvement in regional 'S' wave peak velocity obtained with PW-TDI confirmed the previous observation [31].

After bariatric surgery, left ventricular diastolic functional improvement was demonstrated in the mitral flow velocities and times and in PW-TDI mitral annulus velocities in our obese patients [31]. Early and late phases of diastole improved, too.

Weight loss after bariatric surgery appears to be able to induce an improvement in volume overload (reduction in enddiastolic volume), a reduction in LVM [32–34] and a better intrinsic myocardial contractility and deformability, probably mediated by a better insulin/glucose interaction (trend to normalization of HOMA). In these patients, the normalization of insulin resistance may be essential to substantially reduce the risk of congestive heart failure [8].

Strengths and Limitations

A limitation of this study is represented by the low number of patients; however, this group, being part of a larger class III obese population [12, 13], matched perfectly with the control group (case-control study). The lack of myocardial biopsy is another limitation of the study but in our opinion it is not ethically acceptable in these patients.

Conclusion

Bariatric surgery appears to be efficient not only for a substantial and durative weight loss but also to improve in myocardial metabolism and function. This study establishes the utility of the new ultrasonic techniques to detect very early structural and functional myocardial alterations and their regression after bariatric surgery in obese patients. Further studies are required to confirm these findings in a larger patient population, extending the research to the complex interactions between obesity (even in classes I and II), potential comorbidities (arterial hypertension, diabetes and nocturnal sleep apnea), risk factors (C-reactive protein), humoral factors (leptin, interleukins and adiponectin) and myocardial metabolism and function.

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References

1 Flegal KM, Carrol MD, Ogden CL, Johnson CL: Prevalence and trends in obesity among US adults, 1999–2000. JAMA 2002;288:1772–1773.

2 Poirier P, Giles TD, Bray GA , Hong Y, Stern JS, Pi-Sunyer FX, Eckel RH: Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Circulation 2006;113:898–918.

3 Poirier P, Alpert MA: Heart disease; in Eckel RH (ed): Obesity: Mechanisms and Clinical Management. Philadelphia, Williams & Wilkins, 2003, pp 181–201.
4 Clinical Guidelines on the Identification, Evaluation and Treatment of Overweight and Obesity in Adults – The Evidence Report. National Institutes of Health. Obes Res 1998;6(suppl 2):51S–209S.
5 Kenchaiah S, Evans JC, Levy D, Wilson PW, Benjamin EJ, Larson MG, Kannel WB, Vasan RS: Obesity and the risk of heart failure. N Engl J Med 2002;347:305–313.
6 Rutter MK, Parise H, Benjamin EJ, Levy D, Larson MG, Meigs JB, Nesto RW, Wilson PW, Vasan RS: Impact of glucose intolerance and insulin resistance on cardiac structure and function: sex-related differences in the Framingham Heart Study. Circulation 2003; 107:448–454.
7 Ferrannini E, Natali A, Belli P, Cavallo-Perin P, Lalic N, Mingrone G; European Group for the Study of Insulin Resistance (EGIR): Insulin resistance and hypersecretion in obesity. J Clin Invest 1997;100:1166–1173.
8 Ingelsson E, Sundström J, Ärnlöv J, Zethelius B, Lind L: Insulin resistance and risk of congestive heart failure. JAMA 2005;294: 334–341.
9 Unger R: Minireview: weapons of lean body mass destruction: the role of ectopic lipids in the metabolic syndrome. Endocrinology 2003;144:5159–5165.
10 Szczepaniak L, Dobbins R, Metzger G, Sartoni-D'Ambrosia G, Arbique D, Vongpatanasin W, Unger R, Victor RG: Myocardial triglycerides and systolic function in humans: in vivo evaluation by localized proton spectroscopy and cardiac imaging. Magn Reson Med 2003;49:417–423.
11 Wong Chiew Y, O'Moore-Sullivan T, Leano R, Byrne N, Beller E, Marwick TH: Abnormalities of left ventricular myocardial characteristics associated with obesity. Circulation 2004;110:3081–3087.
12 Di Bello V, Santini F, Di Cori A, Pucci A, Palagi C, Delle Donne MG, Fierabracci P, Marsili A, Talini E, Giannetti M, Biadi O, Balbarini A, Mariani M, Pinchera A: Obesity cardiomyopathy: is it a reality? An ultrasonic tissue characterization study. J Am Soc Echocardiogr 2006;19:1063–1071.
13 Di Bello V, Santini F, Di Cori A, Pucci A, Palagi C, Delle Donne MG, Giannetti M, Talini E, Nardi C, Pedrizzetti G, Fierabracci P, Vitti P, Pinchera A, Balbarini A: Relationship between preclinical abnormalities of global and regional left ventricular function and insulin resistance in severe obesity: a color Doppler imaging study. Int J Obes 2006;30: 948–956.
14 Hooge J, Heimdal A, Jamal F, Kukulski T, Bijnens B, Rademakers F: Regional strain and SR measurements by cardiac ultrasound: principles, implementation and limitations. Eur J Echocardiogr 2000;1:154–170.
15 Christou NV, Sampalis JS, Liberman M, Look D, Auger S, McLean AP, MacLean LD: Surgery decreases long-term mortality, morbidity, and health care use in morbidly obese patients. Ann Surg 2004;240:416–423.
16 Jan JC, Hong D, Pereira N, Patterson EJ: Laparoscopic adjustable gastric banding versus laparoscopic gastric bypass for morbid obesity: a single-institution comparison study of early results. J Gastrointest Surg 2005;9:30–39.
17 Crepaldi G, Belfiore F, Bosello O, Cavizel F, Contaldo F, Enzi G, Melchionda N: Italian Consensus Conference – overweight, obesity and health. Int J Obes 1991;15:781–790.
18 Wallace TM, Matthews DR: The assessment of insulin resistance in man. Diabet Med 2002;19:527–534.
19 Nagueh SHF, Middleton KJ, Kopelen HA, Zoghbi WA, Quinones MA: Doppler tissue imaging: a noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. J Am Coll Cardiol 1997;30:1527–1533.
20 Weidemann F, Jamal F, Sutherland GR, Claus P, Kowalski M, Hatle L: Myocardial function defined by strain rate and strain during alterations in inotropic states and heart rate. Am J Physiol Heart Circ Physiol 2002;283:H792–H799.
21 Bland JM, Altman DG: Measurement error and correlation coefficients. BMJ 1996;313: 41–42.
22 Di Bello V, Giorgi D, Talini E, Dell'Omo G, Palagi C, Romano MF, Pedrinelli R, Mariani M: Incremental value of ultrasonic tissue characterization (backscatter) in the evaluation of left ventricular myocardial structure and mechanics in essential arterial hypertension. Circulation 2003;107:74–80.
23 Di Bello V, Giorgi D, Viacava P, Talini E, Nardi C, Palagi C, Delle Donne MG, Verunelli F, Mariani MA, Grandjean J, Dell'Anna R, Di Cori A, Zucchelli G, Romano MF, Mariani M: Severe aortic stenosis and myocardial function: diagnostic and prognostic usefulness of ultrasonic integrated backscatter analysis. Circulation 2004;110:849–855.
24 Iacobellis G, Ribaudo MC, Leto G, Zappaterreno A, Vecci E, Di Mario U, Leonetti F: Influence of excess fat on cardiac morphology and function: study in uncomplicated obesity. Obes Res 2002;10:767–773.
25 Peterson LR, Waggoner AD, Schechtman KB, Meyer T, Gropler RJ, Barzilai B, Davila-Roman VG: Alteration in left ventricular structure and function in young healthy obese women. J Am Coll Cardiol 2004;43: 1399–1404.
26 Bray GA: Risks of obesity. Endocrinol Metab Clin North Am 2003;32:787–804.
27 Grundy SM: Obesity, metabolic syndrome, and cardiovascular disease. J Clin Endocrinol Metab 2004;89:2595–2600.
28 Sowers JR: Obesity as a cardiovascular risk factor. Am J Med 2003;115:37S–41S.
29 Ahmed Q, Chung-Park M, Tomashefski JF Jr: Cardiopulmonary pathology in patients with sleep apnea/obesity hypoventilation syndrome. Hum Pathol 1997;28:264–269.
30 MacMahon SW, Wilcken DE, Macdonald GJ: The effect of weight reduction on left ventricular mass. A randomized controlled trial in young, overweight hypertensive patients. N Engl J Med 1986;314:334–339.
31 Willens HJ, Chakko SC, Byers P, Chirinos JA, Labrador E, Castrillon JC, Lowery MH: Effects of weight loss after gastric bypass on right and left ventricular function assessed by tissue Doppler imaging. Am J Cardiol 2005;95:1521–1524.
32 Alpert MA, Lambert CR, Terry BE, Cohen MV, Mulekar M, Panayiotou H, Mukerji V: Effect of weight loss on left ventricular diastolic filling in morbid obesity. Am J Cardiol 1995;76:1198–1201.
33 Karason K, Wallentin I, Larsson B, Sjostom L: Effects of obesity and weight loss on cardiac function and valvular performance. Obes Res 1998;6:422–429.
34 Kanoupakis E, Michaloudis D, Fraidakis O, Parthenakis F, Vardas P, Melissas J: Left ventricular function and cardiopulmonary performance following surgical treatment of morbid obesity. Obes Surg 2001;11:552–558.