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Cardiac systolic and diastolic function can be improved and epicardial fat can be decreased over a very short period of time in obese patients without heart disease by the very low calorie diet

Abstract

Objective: The objective of the study was to evaluate the effect of an eight week period of very low calorie diet (VLCD) on heart function and amount of epicardial adipose tissue in obese people without heart disease.

Methods: Fifty-two obese patients (38 women, 14 men, mean age 47.6±12.3years, mean BMI 46.2±7.0kg/m^2) were assigned to a VLCD enriched with vegetables for eight weeks. Transthoracic echocardiography was performed before and after the diet period. Left ventricular size, ejection fraction, diastolic function, left and right ventricular myocardial performance index (MPI) and thickness of epicardial adipose tissue were measured. Heart rate, blood pressure and plasma glucose and triglyceride concentration were also analysed.

Results: During the diet period the BMI decreased from 46.2±7.0kg/m^2 to 41.8±6.1kg/m^2 ($p<0.0001$). The left ventricular MPI decreased from 0.42±0.07 to 0.37±0.07 ($p<0.0001$) and right ventricular MPI decreased from 0.30±0.09 to 0.27±0.09 ($p=0.0256$) showing significant systolic and diastolic improvement in the performance of both ventricles. The thickness of epicardial fat decreased from 4.4±1.5mm to 3.4±1.4mm ($p<0.0001$). The heart rate decreased from 75.8±9.7beats/min to 67.0±10.3 beats/min ($p<0.0001$) and the systolic blood pressure decreased from 140±14.3mmHg to 135.2±10.6mmHg ($p=0.0087$). The plasma glucose concentration decreased from 6.71±1.96mmol/l to 6.02±1.59mmol/l ($p<0.0001$). The plasma triglyceride concentration decreased from 1.77±0.89mmol/l to 1.36±0.68mmol/l ($p=0.0002$).

Conclusion: VLCD caused during only eight weeks period significant reduction in BMI as well as in the amount of epicardial fat and significant improvement in the systolic and diastolic function of both ventricles in obese persons.

Keywords: obesity, cardiac performance, myocardial performance index, very low calorie diet, epicardial fat, pericardial fat, weight reduction

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Abbreviations: NS, not significant; MPI, myocardial performance index; ET, ejection time; IVCT, isovolumic contraction time; IVRT, isovolumic relaxation time; e', early velocity of mitral annulus; a', late velocity of mitral annulus; BMI, body mass index; HDL, high density lipoprotein; P, statistical significance

Introduction

Obesity is a major risk factor for cardiovascular diseases.[1–3] Obesity also represents an independent risk factor for congestive heart failure.[4,5] The haemodynamic hallmarks of obesity, increased heart rate and stroke volume, are thought to be a compensatory adaptation to increased adipose tissue mass at the expense of left ventricular remodelling, which can later progress to heart failure.[6] Increasing obesity is associated also with increasing severity of right ventricular dysfunction in overweight and obese subjects independent of sleep apnea.[7] Fatty heart (cor adiposum) often seen in obese persons has been known for more than 300years.[6] Obesity has reached pandemic proportions.[2,3,6] Because of these well known facts it is of great importance to study obesity related cardiac functions. The objective of this study was to evaluate the effect of an eight week period of VLCD on heart function and the amount of epicardial adipose tissue in obese people without heart disease. Transthoracic echocardiography was used as a method for analysing cardiac function[8–12] and to measure the amount of epicardial fat.[13]

Methods

Subjects

Fifty-two consecutive obese patients who could successfully complete eight weeks VLCD were enrolled in this study between the years 2005-2008. Their mean age was 47.6±12.3years and mean BMI was 46.2±7.0kg/m^2. There were 38 women and 14 men. The exclusion criteria were cardiac disease, type 1 diabetes, kidney disease and serious mental problems. The demographics of the patients are seen in detail in Table 1.

Diet

The subjects were assigned to a VLCD for eight weeks. The diet consisted of commercially available VLCD- products (Nutrilett®, Allevo®). All the VLCD formulas contained protein of soya. Other main ingredients in the formulas were fiber of soya, oil of soya, powder of milk, fiber of oats and oil of raps. The content of the VLCD formulas is seen in detail in Table 2.

Table 1 Baseline characteristics of the study participants (n=52)

Age (range)	47.6±12.3 (16-70) years
Sex: Female/male	38/14
BMI (range)	46.2±7.0 (33.1-65.0)
Weight (range)	134.0±24.7 (91-192) kg
Number of patients with hypertension	28/52 (54%)
Number of patients with type 2 diabetes	24/52 (46%)
Number of patients with impaired fasting glycaemia (IFG)	6/52 (12%)
Number of patients with medication	38/52 (73%)
ACE inhibitors or ARB:s	28/52 (54%)
Diuretics	18/52 (35%)
Betablockers	10/52 (19%)
Calcium channel blockers	6/52 (12%)
Other antihypertensive agents	3/52 (6%)
Lipid lowering agents	18/52 (35%)
Insulin	4/52 (8%)
Oral glucose lowering agents	21/52 (40%)
Acetosalisylic acid	19/52 (37%)

Table 2 The daily content of energy and nutrients received from the VLCD formulas. Additional vegetables are not included in this table. Nutriton of women consisted of five units of VLCD formula and men had six units. There were some variations in the contents of the formulas

Nutrient	Women	Men
Energy Kcal	545-555	654-666
Protein g	58-66	70-79
Carbohydrates g	52-68	62-82
Total fat g	13	16
Saturated fat g	5	6
Linoleic acid g	3,0-3,7	3,6-4,4
Linolenic acid g	0,4-0,5	0.5-0,6
Fiber g	18-23	22-28
Sodium g	1,4-2,5	1,7-3,0
Vitamin A µg	1000	1200
Vitamin D3 µg	5	6
Vitamin E µg	10	12
Vitamin K1 µg	70	84
Vitamin C µg	60	72
Thiamine mg	1,4	1,7
Riboflavin mg	1,7-2,3	2,0-2,8
Niacin mg	18	22
Vitamin B6 mg	2,1	2,5
Folic acid µg	300	360
Vitamin 12 µg	3,0	3,6
Biothine µg	100-150	120-180
Pantothenic acid mg	4-6.	5-7.
Calcium mg	900	1080
Phosphorous	700-800	840-960
Iron mg	16	19
Magnesium mg	350	420
Zinc mg	12-15.	14-18.
Copper mg	2,0	2,4
Iodine µg	150	180
Manganese mg	2,5	3,0
Chromium µg	50	60
Selene µg	50-55	60-66
Molybdene µg	150	180
Potassium g	1,9	2,3
Chloride g	1,7	2,0

In addition to the VLCD formulas the following vegetables were allowed freely during the diet: tomato, cucumber, lettuce, carrot, white cabbage, red cabbage, Brussels sprouts, leek, spinach, broccoli, parsley, sweet peppers, celery, cauliflower, radishes, Chinese cabbage and squash. Coffee, tea and light sodas were allowed. Alcohol was excluded. The estimated total amount of calories was 700-900kcal/day.

No new medication was initiated at the beginning or during the VLCD. There were also no increased dosages of any medicine compared to the initial dosages. The amounts of the diuretics, glucose lowering agents and lipid lowering agents were reduced during the VLCD. The level of plasma glucose was followed carefully at regular intervals by the diabetic patients.

The eight week period of VLCD was chosen because it was a routine intervention in the treatment of severe obesity in the hospital. All VLCD formulas were bought by the patients themselves and they could choose between the two available products (Nutrilett® or Allevo® as they were sold in the year 2005). No contact was made to the manufacturers of these formulas. No financial support was thus received for anyone connected to this study. The compliance was based on the weekly visits to a nurse, where the patients were weighed and interviewed.

Echocardiography

A two-dimensional Doppler echocardiographic examination was performed before and after the diet period. Parasternal long-axis views were used for measuring left ventricular cavity size and ejection fraction and left atrial diameter. Pulsed wave (H4.0 MHz) Doppler transmitral and transtricuspid flow images were acquired from the apical four-chamber view at the mitral and tricuspid leaflet tips. Left ventricular ejection time was obtained by pulsed wave Doppler in the left ventricular outflow tract of the apical long axis view. Right ventricular ejection time was interrogated by pulsed wave Doppler in the right ventricular outflow tract of parasternal short-axis view. Pulsed Doppler recordings were made at a sweep speed of 100mm/s. The images were recorded digitally (Syngo Dynamics, Siemens Medical System, U.S.A.) for later analysis.

The MPI (Tei index) was calculated as the sum of isovolumic contraction and relaxation times divided by ejection time. For left ventricular MPI Doppler measurements were averaged over five cycles and for right ventricular MPI over three cycles.

Left ventricular annular velocities were recorded from the apical 4-chamber view with pulsed wave Doppler tissue imaging (DTI) with the 5.0mm Doppler sample imaging at the septal and lateral mitral annulus of the left ventricle to obtain early and late mitral annular velocities (e' and a') Both annular velocity values were averaged over three cardiac cycles. The velocity ratio e'/a' recorded from septal annulus was calculated and used for evaluation of left ventricular diastolic function.[12] If recording of velocities from the septal annulus were inadequate the recordings from lateral annulus were used.

Epicardial fat thickness was measured in end diastole on the free wall of the right ventricle from the parasternal long-axis view (2-dimensional) as previously described.[13] Three measurements were averaged for the final result.

All the echocardiograms were obtained by the same physician (ML) with echocardiographic accreditation of European Society of Cardiology. He knew whether the patient was in the beginning of the diet or at the end of the diet. All the echocardiograms were performed by using an ACUSON SEQUOIA C 256 system (Acuson, Mountain View, CA, U.S.A.), using a H 4.0MHz transducer recorded with a simultaneous electrocardiogram.

Haemodynamic measurements

Blood pressure at rest was measured before and after the diet. The heart rate at rest was registered before and after the diet period during the echocardiographic examination.

Laboratory analysis

The fasting plasma glucose level, total cholesterol, high density lipoprotein (HDL) and triglyceride concentration were measured before and after the diet.

Statistical analysis

To compare differences before and after the diet student t tests for paired data were performed. Statistical significance was determined at a p value of <0.05. The study protocol was approved by the Ethics Committee of the Hospital District of Southwest Finland.

Results

BMI decreased from 46.±7.0kg/m^2 to 41.8 ±6.1kg/m^2 (p<0.0001) during the diet period.

Echocardiography

All the patients were in sinus rhythm during echocardiographic recordings. There were no significant changes in the diameter or ejection fraction of left ventricle or in the diameter of left atrium. The left ventricular MPI decreased in 48/52 (92%) patients, remained as the same in 3/52 (6%) and increased in 1/52 (2%) patient. The mean change in the MPI was from 0.42±0.07 to 0.37±0.07 indicating significant systolic and diastolic improvement of left ventricular performance. There was a significant improvement in both components of the left ventricular MPI. The ejection time of the left ventricle increased from 300±19msec to 321±22msec (p<0.0001). The sum of the isovolumic contraction time and isovolumic relaxation time decreased from 125±22msec to 117±23msec (p<0.0001) Table 3.

Table 3 Results of echocardiographic measurements

	Before diet	After diet	Change in %	P
Left ventricular MPI	0.42±0.07	0.37±0.07	11.9	< 0.0001
Left ventricular ET (msec)	300±19	321±22	7	<0.0001
Left ventricular IVCT+IVRT (msec)	125±22	117±23	6.4	<0.0001
Right ventricular MPI	0.30±0.09	0.27±0.09	10	0.0265
Left ventricular e'/a'	1.03±0.29	1.12±0.03	8.74	0.0025
Epicardial fat (mm)	4.4±1.5	3.4±1.4	22.7	< 0.0001
Pericardial fat	2.3±1.8	1.4±1.4	39.1	< 0.0001
Epicardial fat + pericardial fat	6.7±2.7	4.8±2.3	28.4	< 0.0001
Left ventricular diastolic diameter (mm)	54.2±3.7	54.2±3.7	0	NS
Left ventricular ejection fraction (%)	66.5±3.7	66.6±3.8	0.2	NS
Left atrial diameter (mm)	44.7±4.6	44.0±4.7	1.6	NS

NS, not significant; MPI, myocardial performance index; ET, ejection time; IVCT, isovolumic contraction time; IVRT, isovolumic relaxation time; e', early velocity of mitral annulus; a', late velocity of mitral annulus

The corresponding change in the mean values of the right ventricular MPI were from 0.30±0.09 to 0.27±0.09 (p=0.0256). The e'/a' velocity ratio in the left ventricle increased from 1.0±0.29 to 1.12±0.30 (p=0.0025) indicating significant improvement in the diastolic function of the left ventricle. The thickness of the epicardial adipose tissue on the right ventricle was 4.4±1.5mm before and 3.4±1.5mm after the diet (p<0.0001).

Haemodynamic changes

Significant decrease in heart rate was seen during the diet period from 75.8±9.7 beats/min to 67.0±10.3 beats/min ($p<0.0001$). Systolic blood pressure decreased from 140.0±14.3mmHg to 135.2±10.6mmHg ($p=0.0087$) and diastolic from 84.1±9.0mmHg to 81.5±8.1mmHg ($p<0.0436$). The heart rate x systolic blood pressure product decreased from 10605±1718 to 9075±1686 ($p<0.0001$) Table 4.

Table 4 Results of metabolic and hemodynamic findings

	Before diet	After diet	Change in %	P
BMI (kg/m^2)	46.2±7.0	41.8±6.1	9.5	< 0.0001
Heart rate (beats/min)	75.8±9.7	67.0±10.3	11.6	< 0.0001
Systolic blood pressure (mmHg)	140.0±14.3	135.2±10.6	3.4	0.0087
Diastolic blood pressure (mmHg)	84.1±9.0	81.5±8.1	3.1	0.0436
Heart rate (beats/min) x systolic blood pressure (mmHg)	10605±1718	9075±1686	14.4	< 0.0001
Trigly (mmol/l)	1.8±0.9	1.4±0.7	23.2	0.0002
Gluc (mmol/l)	6.7±2.0	6.0±1.6	10.3	< 0.0001
Glycocylated haemoglobin (%)	6.4±1.1	6.0±0.9	6.3	< 0.0001
Total cholesterol (mmol/l)	4.6±1.0	4.3±1.1	6.5	0.0266
HDL/total cholesterol (%)	29.7±7.6	29.9±9.0	0.7	NS
Low density lipoprotein	2.5±0.9	2.5±1.0	0	NS

BMI, body mass index; HDL, high density lipoprotein; P, statistical significance

Laboratory analysis

The fasting plasma glucose decreased from 6.71±1.96mmol/l to 6.02±1.59mmol/l ($p<0.0001$) and triglyceride decreased from 1.77±0.89mmol/l to 1.36±0.68 ($p=0.0002$).

Discussion

We used eight weeks VLCD enriched with vegetables as an intervention method to receive these changes. No patients had diagnosed heart disease but persons with type 2 diabetes and hypertension were included in the study group. The changes of the diet in our study were clear caloric restriction, decrease in the amount of fat and carbohydrates, increase in the amount of soyaprotein and guaranteed amounts of daily allowances of micronutrients and increase in percentage of the daily calories received from the vegetables.

This study showed significant improvement in both systolic and diastolic cardiac functions of both ventricles in obese persons after eight weeks of VLDC. These persons had no heart disease and had normal ejection fractions at rest. It also shows clear decrease of epicardial fat at the same time and also this change occurred rapidly than previously reported. To our knowledge this is the first study that simultaneously shows these changes in that period of time after the change of diet.

At the same time significant beneficial haemodynamic changes, decrease in heart frequency and blood pressure, happened and the improvement of rate-pressure product suggested decreased cardiac workload. Also BMI reduction of 9.5% occurred in these patients and the blood fasting glucose and triglyceride levels decreased significantly.

Morbid obesity is a high-output state[6] which includes also hyperkinetic systole[14,15] with high ejection fraction of left ventricle at rest.[16] Therefore, the use of mere ejection fraction and its equivalents as a measure of change in left ventricular systolic function is controversial in persons without heart disease and therefore we used echocardiographic determination of MPI, as an indicator of change in cardiac function. MPI combines both systolic and diastolic functions and is a measure of effectiveness of cardiac cycle[17] and offers an accurate method to study early changes in cardiac performance.[18]

Few clinical studies have shown a relationship between changes in cardiac function and dietary changes in obese persons.[19] Weight loss can be associated with improved left ventricular diastolic function[19–27] but improvement in left ventricular systolic function at rest has before our study been confined to those with depressed systolic function at baseline.[19,22,27] Even after bariatric surgery which often causes substantial weight loss, improvement of systolic function has been limited to those with depressed left ventricular systolic function before surgery.[19,28,29]

Theoretical plausible mechanisms may explain this rapid change in cardiac function seen in our study. It has been discussed whether the caloric restriction or weight loss itself plays the key role in the improvement of diastolic function.[30,31] Riordan et al.,[31] have shown that a yearlong caloric restriction or increase of exercise leading to weight loss can improve left ventricular diastolic function in healthy non-obese persons. Meyer et al.,[30] have shown that long-term caloric restriction ameliorates the age-associated decline in diastolic function in healthy, non-obese individuals. Hammer et al.,[24] have shown improved diastolic function after a 16-week caloric restriction in obese patients with diabetes mellitus type 2. The weight loss in these patients was over 20% during the diet (VLCD).

In general, caloric restriction with adequate nutrition intake can cause metabolic adaptations including decreased metabolic, hormonal and inflammatory risk factors for diabetes and cardiovascular disease.[32–34] Caloric restriction has been proposed[35] to increase bioavailability of NO and inhibit inflammatory pathways thus suppressing initiation or progression of vascular disease.

Fatty infiltration of cardiomyocytes has been reported in obese patients with heart failure[6,36] and the amount of myocardial fat has

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been shown to correlate with the amount of epicardial fat.[37] In obese diabetics[24] myocardial triglyceride content decreased and diastolic function improved after weight loss over 20%. In the study of Viljanen et al.,[38] caloric restriction with VLCD for six weeks decreased myocardial triglyceride content by 31%. Fatty heart can be prevented by lifestyle modification and interventions, so it is important to recognize its existence as early as possible.[6]

The anatomical close connection between excess epicardial fat and myocardium might increase the weight of the ventricles thus increasing the effort involved in pumping and also allow the local paracrine hormonal interaction between epicardial adipose tissue and myocardium.[39,40]

The epicardial fat is metabolically active visceral fat[13] and a source for inflammatory mediators.[41] It could be speculated that the amount of metabolically active fat that is abolished adjacent to the cardiac muscle could cause the positive change. Some harmful metabolites could disappear from the area very near the cardiac muscle.

In our study the improvement in the cardiac systolic and diastolic function occurred rapidly, much more rapidly than one could expect based on traditional concept of the functions of the heart. In our study the relative improvement in heart function and relative decrease in epicardial fat were bigger than the relative decrease of BMI thus together with rapid change suggesting again that metabolic changes might play bigger role than the weight loss itself. Most patients remained very obese also afterwards suggesting that the weight loss itself cannot alone explain this success.

The method to receive this improvement is physiological, low-cost and can be achieved with little medical supervision and without any exercise plan. The change in the composition of the diet was drastic. Obviously drastic changes in the diet can cause drastic changes in cardiac function even in the short term.

Conclusion

Caloric restriction with VLCD caused after only eight weeks of diet a significant improvement in the cardiac systolic and diastolic performance and a reduction of epicardial fat in obese persons. At the same time beneficial haemodynamic changes occurred as well as a significant reduction in BMI. It is unclear how generalizable these results are. Further study is needed. These fast results might offer new motivations to weight loss efforts and approaches into the prevention of the heart failure in obese persons.

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Conflict of interest

The author declares no conflict of interest.

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