PANMINERVA MED 2000;42:123-9

Effects of a short-term hypoenergetic diet on morphofunctional left ventricular parameters in centrally obese subjects

An echocardiographic study

S. CORRAO, S. ARNONE, R. SCAGLIONE, V. AMATO, G. AMICO, A. LICATA, G. LICATA

From the Institute of Internal Medicine
University of Palermo, Palermo, Italy

Background. **We aimed to study centrally obese subjects without other diseases, to establish whether a short-term hypoenergetic balanced regimen is able to positively modify left ventricular (LV) patterns.**

Methods. **We studied 32 obese subjects (out of 52 recruited for this study) with central fat distribution and without associated diseases. Each subject had undergone a moderately hypoenergetic diet for a four-month follow-up period and had a regular loss in weight. Some relevant clinical and echocardiographic parameters were evaluated. Baseline data and those evaluated at the end of the follow-up period were used for outcome analysis.**

Results. **We found a considerable reduction in LV mass and other LV structural parameters including relative wall thickness (RWT). Moreover, we found an improvement of both LV ejection fraction and filling parameters. As regards the relation ship between parameter changes, LV mass was correlated to LV internal diameter and mainly to LV wall thickness. LV mass change was also correlated to a reduction of diastolic BP and RWT. Only improvements in LV filling were correlated to WHR reduction. None of the changes in cardiac variables resulted significantly correlated to BMI change. Other interesting correlations are reported in the text.**

Conclusions. **Our study points out that improvements in LV structure and function are rapidly possible with a moderately hypoenergetic regimen in obese otherwise healthy subjects. The main changes were those in LV wall thickness even if a more complex cardiovascular adjustment was recognised. All this could be very important to possibly prevent future cardiovascular events (including heart failure), so largely linked to obesity of central type.**

KEY WORDS: Obesity - Ventricular left function - Diet - Echocardiography.

Several studies show a significant association of obesity with cardiovascular morbidity and mortality.[1,2]

It is also well known that obesity is often associated with modifications in cardiac function and/or left ventricular structure (*i.e.*, the presence of left ventricular hypertrophy even in the absence of systemic hypertension).[3,4]

Previous studies[5-8] report the presence of diastolic and systolic left ventricular abnormalities in mildly and moderately obese subjects, without any associated complaint. Alpert *et al.*[9] report an impaired response to exercise of left ventricular systolic function in morbidly obese subjects. On the other hand, our previous data also support the suggestion that obesity could represent an independent risk factor for congestive heart failure after a long-term incubation period. In fact we have found an inverse correlation between the duration of obesity and both left ventricular ejection fraction at peak exercise[10] and left ventricular ejection fraction at rest.[5]

Received July 5, 1999.
Accepted for publication February 14, 2000.

Address reprint requests to: S. Corrao, Via dei Nebrodi 67, 90144 Palermo, Italy. E-mail: s.corrao@tiscalinet.it

However, human obesity is not a homogeneous condition. Several investigations show that there are relevant pathophysiological and clinical differences between central and peripheral adipose distribution.[11 12]

The central excess of body adipose tissue appears to be associated with a complex endocrine aberration,[11 12] hyperactivity of the hypothalamo-pituitary-adrenocortical axis[13 14] and derangement of sex steroid hormone secretions.[15-17]

Moreover central obesity increases the risk for cardiovascular disease[18 19] while there is little evidence regarding the relatioship between peripheral obesity and cardiovascular risk.

Many studies on hypertensive subjects show that a decrease in body weight is associated with both a fall in blood pressure and a reduction of left ventricular mass.[20-22]

Nevertheless, there are no satisfactory data about hemodynamic and structural cardiovascular changes after weight loss by a hypoenergetic regimen in moderately centrally-obese otherwise healthy subjects.

The purpose of our investigation was to study these changes in moderately obese subjects with central fat distribution and without misleading factors (*i.e.* hypertension, diabetes mellitus, impaired glucose tolerance, evident lipid abnormalities and any other associated complaint) to establish whether a short-term balanced hypoenergetic regimen was able to positively modify cardiovascular structural and hemodynamic patterns.

Materials and methods

Subject selection and study procedure

Obese subjects were recruited from all obese individuals attending the obesity centre of Internal Medicine Division at the University of Palermo, Italy.

Elegibility criteria for the selection phase were: 1) age <50 years; 2) overt obesity according to the Italian Consensus Conference guidelines (which corresponds to a BMI value ≥30.5 kg/m^2 for men and ≥27.3 kg/m^2 for women;[23] 3) waist-hip ratio values according to the Italian Consensus Conference cut-off points indicating visceral fat distribution (WHR ≥0.92 for men and >0.81 for women), and 4) blood pressure values into the normal range (DBP <90 mmHg and SBP <140 mmHg) according to the Joint National Committee on detection, evaluation, and treatment of high blood pressure criteria[24 25] on at least three visits in three consecutive weeks.

All the subjects who met the above-mentioned criteria were submitted to an assessment consisting of a medical history, physical examination, resting electrocardiogram, chest X-ray, M-mode and cross-sectional echocardiography, and routine laboratory studies.

Then we excluded all the subjects with a history and/or clinical findings of both overt cardiac and extracardiac diseases and with a positive history of body weight cycling during the last year. Moreover we also excluded all subjects with poor quality echocardiograms that did not permit a reliable evaluation of left ventricle internal dimensions and both septal and posterior wall thickness (that is when appropriate echocardiographic tracing did not permit a clear identification of left ventricle endocardial outlines).

Fifty-two subjects entered the follow-up program: 22 women and 30 men (average age ± 1 standard deviation = 36.4±7.7 years). All of them were in sinus rhythm. All the subjects were informed of the purpose of the study and gave their consent. The study was conducted in accordance with the declaration of Helsinki (1983) and Tokyo and was approved by our Institutional Ethical Committee.

During the follow-up period, which lasted for about four months, all patients regularly visited the outpatient clinic every four weeks. At each visit, blood pressure and weight were measured; all were interviewed by the same dietician to ensure compliance with the dietary program and all were seen by the physician for follow-up determination of their clinical status.

Dietary program

The daily diet contained about 5439 megajoules for men and 4602 megajoules for women. The diet consisted of about 55% carbohydrates, 28% lipids and 17% proteins.

After an interview by a dietician, specific dietary components were individually tailored to each patient on the basis of individual body size and dietary habits. Then, a nutritionally balanced diet was designed interfering as little as possible with food preferences. It was a mediterranean regimen (divided into three meals: breakfast, lunch and dinner) including milk (only at breakfast), pasta (only at lunch), meat or fish, olive oil, vegetables, bread and fresh fruit. Daily dietary sodium intake ranged between 100 and 200 mmol.

Clinical measurements

Body weight.—Recorded on a level balance scale to the nearest 0.1 kg, with the patient wearing no shoes and clothes.

Height.—Measured by a metal height scale attached to the weight scale.

Blood pressure.—Measured with the patient in recumbent position by a mercury cuff sphygmomanometer as mean of three consecutive measurements, using a cuff of appropriate size.

Diastolic blood pressure was determined as Korotkoff phase V.

Heart rate.—Measured in supine position by electrocardiogram monitoring as mean of five-minute period.

Waist-hip ratio (WHR).—Measured as waist circumference/hip circumference.

Echocardiographic measurements

Between 8.00 and 10.00 hrs, a standard two-dimensional, M-mode and Doppler echocardiographic examination was carried out on each subject standing in a partial left lateral recumbent position. A computer aide ultrasonoscope (ESAOTE BIOMEDICA, via di Caciolle, 15 - 50127 Firenze - Italy) equipped with 2.5 and 3.5 MHz phased-array transducers was used. Transducers are capable of continuous Doppler activity and have pulsed Doppler capacity with a moveable Doppler cursor and an adjustable sample volume size (set at 4 mm for this study).

A two-dimensional echocardiographic study was performed including short-axis views at the levels of the mitral valve and apical four and two chamber views to exclude regional wall motion abnormalities.[26] Standard M-mode echocardiographic examination guided by two-dimensional echocardiography from the left parasternal window was performed. Septal and posterior wall thicknesses, and left ventricular internal diameters were measured according to the standard measurements convention of the American Society of Echocardiography including the thickness of the endocardial echoes.[27] Measurements were made according to the Penn convention and left ventricular mass was calculated with the formula of Devereux and Reichek:[28,29] left ventricular mass (g)= 1.04 [diastolic left ventricular internal diameter + diastolic interventricular septal thickness + diastolic posterior wall thickness)^3] - (diastolic left ventricular internal diameter)^3 - 13.6. Measurement points were taken at the peak of the R wave on the simultaneous electrocardiogram on an average of four cycles.

Left ventricular end-diastolic and end-systolic volumes were calculated from the apical four-chamber view, using the ellipsoid single-plane algorithm.[30] End-diastolic and end-systolic frames from five consecutive beats were selected and the endocardial outlines were traced. Both mean left ventricular volumes and ejection fraction were automatically calculated by the echocardiograph processing system. In our laboratory left ventricular volumes and ejection fraction calculated on five consecutive beats permitted optimal reproducibility and accuracy.[31,32]

We also carried out a standard pulsed and continuous Doppler echocardiographic examination[33] to exclude pathological spectral flow patterns (valve regurgitation and/or stenosis).

Left ventricular inflow tract study

Pulsed Doppler examination of transmitral blood flow was performed, as previously described,[34] from the apical four chamber view on subjects in partial left lateral recumbent position. The sample volume was positioned at the level of the mitral annulus and the cursor oriented parallel to an imaginary line bisecting the left ventricle from apex to mitral valve.

We measured the following variables: the RR' interval, peak E and A velocities, and the deceleration half-time of early diastolic rapid inflow.[35] All the Doppler measurements are the average of 3 cardiac cycles detected at end expiration.

Computed measurements

Body mass index (BMI)=Weight in kg/(height in m)^2.

Left ventricular mass index=Left ventricular mass/Body surface area.

Left ventricular mass/height=Left ventricular mass in g divided by height in m.

Mean blood pressure=Diastolic blood pressure+1/3 × Pulse blood pressure.

Ejection fraction=[(Left ventricular diastolic volume-Left ventricular systolic volume)/Left ventricular diastolic volume] × 100.

A/E ratio=(Peak A/Peak B) × 100.

Deceleration half time/RR'=Deceleration half time

TABLE I.—*Effects of weight reduction on clinical and left ventricle morphological data (mean value ±1 SD).*

Parameters	Baseline	Follow-up	p<*
Body mass index (kg/m^2)	36.6±5.2	33.4±4.1	0.001
Weight (kg)	102±13	93±9	0.001
Waist hip ratio	0.98±0.08	0.88±0.05	0.001
LV internal diameter in diastole (mm)	53±4	51±5	0.001
LV internal diameter in systole (mm)	37±5	34±4	0.001
IV septal thickness (mm)	8±1	7±1	0.001
Posterior wall thickness (mm)	8±2	7±1	0.002
LV mass (g)	158±33	130±30	0.001
LV mass index (g/m^2)	76±15	64±13	0.001
LV mass/height (g/m)	95±21	77±18	0.001
Relative wall thickness	0.30±0.05	0.27±0.04	0.003

LV=left ventricular; IV=interventricular. *By Wilconxon matched-pairs signed rank test.

TABLE II.—*Effects of weight reduction on both functional parameters and transmitral Doppler measurements (mean value ±1 SD).*

Parameters	Baseline	Follow-up	p<*
Systolic BP (mmHg)	132±7	123±6	0.001
Diastolic BP (mmHg)	86±5	78±4	0.001
Heart rate (b/min)	72±9	64±7	0.001
LV ejection fraction (%)	58±4	66±4	0.001
Peak A velocities (m/s)	0.59±0.14	0.57±0.13	ns
Peak E velocities (m/s)	0.56±0.11	0.71±0.14	0.001
A/E ratio (%)	109±28	81±16	0.001
Deceleration half time	145±24	121±13	0.001
Deceleration half time/RR (*1000)	176±43	130±22	0.001

BP=blood pressure; LV=left ventricular. *By Wilconxon matched-pairs signed rank test. ns=not significant.

divided by RR' electrocardiogram interval (in ms) × 1000.

Data analysis

Baseline data and those ones evaluated at the end of the follow-up period were used for analysis. All the echocardiographic measurements were made on digitised images by measuring functions of the echocardiograph processing unit. Averages were automatically calculated. Echocardiograms were analysed by two trained physicians without knowledge of clinical data (all variables reported had an intraobserver coefficient of variability ≤5% and an interobserver one ≤10%). Statistical analysis was conducted with the use of the SPSS for Windows. Values are reported as mean ± Standard Deviation. The Wilcoxon matched-pairs signed-rank test was used to compare baseline values with follow-up values. The change of a variable, for each subject, was computed as follows: baseline value minus the value at follow-up except for peak-E velocity changes that were computed as the latter value minus the former one. Partial correlation coefficients were estimated to examine the relation between the changes of two parameters, adjusting for the linear effects of one or more additional variables.[36]

Results

Two subjects did not complete the follow-up program; 18 subjests (10 men/8 women) had a sparse adherence to hypoenergetic regimen (that is, a weight loss lower than 5% at the end of the study, or a steady weight, or a weight gain and/or weight cycling). These data were not incorporated in all outcome analysis. However, in these 18 subjects, we found no statistically significant changes in any of the measurements.

On the other hand, 32 subjects (18 men/14 women) had a regular loss in weight during the follow-up period. The weight loss was more than 5% at the end of the study compared with the baseline weight. Only the data of these 32 subjects were incorporated in all outcome analysis. Average age was 35.4±9.2 years.

There were considerable changes in the majority of measurements after weight loss as shown in Tables I and II. Only Peak A velocity of transmitral blood flow did not significantly change at follow-up (Table II).

Partial correlation analysis (controlling for gender and age)

Left ventricular mass change was mainly correlated to left ventricular wall thickness change (Table III) and it did not significantly correlate to the changes of any left ventricular filling parameter. Left ventricular mass change was also correlated to diastolic BP change (r=0.47; p<0.01). Moreover, relative wall thickness change was correlated to both left ventricular mass change (r=0.79; p<0.001) and diastolic BP change (r=0.55; p<0.003). Relative wall thickness change was also negatively correlated to A/E ratio (r=-0.41; p<0.03), DHT (r=-0.54; p<0.003) and DHT/RR (r=-0.65; p<0.001) changes. EF change was correlated to systolic (r=0.60; p<0.001) and diastolic BP (r=0.50; p<0.006) changes.

Heart rate change was correlated to peak E velocity change (r=0.71; p<0.001) but it did not correlate to

TABLE III.—*Partial correlation coefficient analysis controlling for gender and age: change in LV mass* versus *changes in LV diastole internal dimension, IV septal thichness and LV posterior wall thichness.*

Parameters	Change in LV mass	
	r	p<
Change in LV internal dimension in diastole	0.73	0.001
Change in IV septal thichness in diastole	0.82	0.001
Change in LV posterior wall thichness in diastole	0.86	0.001

IV=interventricular; LV=left ventricular.

A/E ratio, deceleration half time and deceleration half time/RR' changes. Moreover, A/E ratio change was correlated to WHR changes (r=0.37; p<0.05). As regards the remaining left ventricular structural and functional changes, none of the changes was significantly correlated to BMI, weight and waist-hip ratio changes.

Discussion and conclusions

Alexander *et al.*[37] demonstrate that circulating blood volume, plasma volume, cardiac output and stroke volume decrease in response to weight loss.

Alpert *et al.*[38] also report on the influence of loading conditions on left ventricular systolic function in morbidly obese subjects before and after weight loss.

Nevertheless, there are little data concerning the effects of weight loss on cardiovascular function in centrally obese otherwise healthy subjects.

Himeno *et al.*[39] more recently studied two groups of obese subjects hypertensive and normotensive. However, only eleven were normotensives and recruited without strict criteria of selection; so that firstly the small number of subjects and secondly the actual possibility of selection BIAS could have led to incomplete or erroneous conclusions. To our knowledge, our study is the first that has investigated the cardiovascular effects of weight loss in a large number of obese normotensive subjects without other misleading factors.

The results of our study showed an improvement in left ventricular ejection fraction that may be referred to an adaptative response to loading condition adjustments, which has the aim of maintaining an adequate stroke volume and cardiac output.

On the other hand, we found an improvement in left ventricular filling in almost all of the 32 obese subjects who had significant weight loss. In fact we found a normalisation in both A/E velocity ratio and deceleration half time (even when adjusted for RR' interval) of early transmitral blood flow.

We think that the reduction in deceleration half time, and deceleration half time/RR', is one of the most important pathophysiological findings. In fact the deceleration half-time, just reflects the fall in the left ventricular pressure during the early diastole, giving us information on left ventricular relaxation in the same way as isovolumic relaxation time (that has not been calculated for lack of reliability in our patient series). Since heart rate change only explained peak-E velocity adjustment and both heart rate and loading condition changes were not correlated to A/E ratio and deceleration half time variations, the improvements in both A/E velocity ratio and deceleration half time (also purified by RR' interval) could reflect an improvement of left ventricular relaxation.[40,41]

At the same time, we have found a substantial reduction of left ventricular mass even when it was normalised to body surface area and height. This change was correlated to reduction in left ventricular diastolic internal dimensions but it was mainly correlated to left ventricular wall thickness reduction. Indeed, at the end of the follow-up period we found a significant decrease in RWT. Consequently, in our patients left ventricular remodelling occurred and not simply a proportional decrease in LV structure. As regards the meaning of all that, we think postloading condition changes were important. In fact, RWT change was positively correlated to BP variation despite the fact that our patient sample was constituted by normotensive subjects. Moreover, EF improved when BP decreased. However BP change explains only 30% of RWT change (r^2=0.30) and only 25-36% of EF change (systolic BP change *vs* EF change, r^2=0.36; diastolic BP change *vs* EF change, r^2=0.25). Then, such a rapid leftventricular remodelling and improvement in EF could almost partially be independent of adjustments in loading condition.

Another finding showed by our data was that a major change in LV structure (see RWT change) was correlated to a minor improvement in some LV filling parameters.

Finally, we did not find any relevant correlation between left ventricular mass variation (even when normalised to body surface area or height) and functional parameter changes. Moreover variations in

weight, BMI and WHR did not prove to be correlated to those parameter changes. Only A/E ratio improvement proved correlated to reduction in WHR.

Hence, left ventricular structural and functional adjustments might occur for a more complex reason rather than simply for a loss in weight or loading condition changes. We think that central distribution of adipose tissue, in these obese subjects, could be a marker of an impaired metabolic response to unbalanced and/or over-feeding leading to an unfavorable cardiovascular re-arrangement at least partially independent of overweight.

In conclusion, our data seem to emphasise the importance of food intake control in obese otherwise healthy subjects. Indeed, we found a consistent improvement in LVM and LV filling parameters after a short term hypoenergetic regimen. All this could be very important to possibly prevent future cardiovascular events (including heart failure), so largely linked to obesity of central type.

Further studies should enable us to better comprehend underlying mechanisms.

References

1. Larsson B, Bjorntorp P, Tibblin G. The health consequences of moderate obesity. Int J Obesity 1981;5:97-116.
2. Bray GA. Complications of obesity. Ann intern Med 1985;103: 1052-61.
3. Messerli FH, Sundgaard-Rise K, Reisin ED, Dreslinski GR, Ventura HO, Oigman W *et al.* Dimorphic cardiac adaptation to obesity and arterial hypertension. Ann Intern Med 1983;99:757-61.
4. Alexander J. The cardiomyopathy of obesity. Prog Cardiovasc Dis 1985:27:325-33.
5. Licata G, Scaglione R, Barbagallo M, Parrinello G, Capuana G, Lipari R *et al.* Effect of obesity on left ventricular function studied by radionuclide angiocardiography. Int J Obesity 1991;15:295-302.
6. De Divitiis O, Fazio E, Petitto M, Maddalena G, Contaldo F, Mancini M. Obesity and cardiac function. Circulation 1981;64:477-82.
7. Garavaglia GE, Messerli FH, Nunez BD, Schmeider RE, Grossman E. Myocardial contractility and left ventricular function in obese patients with essential hypertension. Am J Cardiol 1988;62:594-7.
8. Scaglione R, Dichiara MA, Indovina A, Lipari R, Ganguzza A, Parrinello G *et al.* Left ventricular diastolic and systolic function in normotensive obese subjects: influence of degree and duration of obesity. Eur Heart J 1992;14:738-42.
9. Alpert MA, Singh A, Terry BE, Kelly DL, Viliareai D, Mukerji V. Effect of exercise on left ventricular systolic function and reserve in morbid obesity. Am J Cardiol 1989;9:1478-82.
10. Licata G, Scaglione R, Paterna S, Parrinello G, Indovina A, Dichiara MA *et al.* Left ventricular function response to exercise in normotensive obese subjects: influence of degree and duration of obesity. Int J Cardiol 1992;37:223-30.
11. Bjorntorp P. Abdominal obesity and the development of non-insulin dependent diabetes mellitus. Diabetes Metab Rev 1988;4: 615-22.
12. Kissebah AH, Peiris AN. Biology of regional body fat distribution: Relationship to non-insulin dependent diabetes mellitus. Diabetes Metab Rev 1989;5:83-9.
13. Krotkiewski M, Butruk E, Zembrzuska Z. Les fonctions corticosurrenaies dans les divers types morphologiques d'obesitè. Le Diabète 1966;19:229-33.
14. Licata G, Corrao S, Parrinello G, Scaglione R. Obesity and cardiovascular disease. Ann Ital Med Intern 1994;9(Suppl):1-6.
15. Evans DJ, Hoffmann RG, Kaikhoff RH, Kissebah AH. Relationship of androgenic activity to body fat topography, fat cell morphology, and metabolic aberrations in premenopausal women. J Clin Endocrinol Metab 1983;57:304-10.
16. Seidell JC, Bjorntorp P, Sjostrom L, Kvist H, Sannerstedt R. Visceral fat accumulation in men is positively associated with insulin, glucose and C-peptide levels but negatively with testosterone levels. Metabolism 1990;39:897-901.
17. Hartz AJ, Rupley DC, Rimm AA. The association of girth measurements with disease in 32,856 women. Am J Epidemiol 1984;119: 71-9.
18. Bjorntorp P. Obesity and risk of cardiovascular disease (editorial). Acta Med Scand 1985;218:145-7.
19. Larsson B, Svardsudd K, Welin L, Wilhelmsen L, Bjorntorp P, Tibblin G. Abdominal adipose tissue distribution, obesity and risk of cardiovascular disease and death: 13-year follow-up of participants in the study of men born in 1913. Br Med J 1984;288:1401-4.
20. Reisin E, Abel R, Modan M, Silverberg DS, Eliahou HE, Modan B. Effect of weight loss without salt restriction on the reduction of blood pressure in overweight hypertensive patients. N Engl J Med 1978;298:1-6.
21. Fagerberg B, Berglund A, Andersson OK, Berglund G, Wikstrand J. Cardiovascular effects of weight reduction *versus* antihypertensive drug treatment: a comparative, randomised, 1-year study of obese men with mild hypertension. J Hypertens 1991;9:431-9.
22. MacMahon SW, Wilcken DEL, MacDonald GJ. The effect of weight reduction on left ventricular mass. A randomised controlled trial in young, overweight hypertensive patients. N Eni J Med 1986;314:334-9.
23. Crepaldi G, Belfiore F, Bosello O, Caviezel F, Contaldo F, Enzi G *et al.* Special report: Italian Consensus Conference – overweight, obesity and health. Int J Obes 1991;15:781-90.
24. The 1993 Report of Joint National Committee on detection, evaluation and treatment of high blood pressure. Arch Intern Med 1993;153:154-83.
25. The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. Arch Intern Med 1997;157(21):2413-46.
26. Parisi AF, Moynihan PF, Folland ED, Feldman CL. Quantitative detection of regional left ventricular contraction abnormalities by two-dimensional echocardiography. II Accuracy in coronary heart disease. Circulation 1981;63:761-7.
27. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendation regarding quantitation in m-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072-3.
28. Devereux RB, Reichek N. Echocardiographic determination of left ventricular mass in man. Anatomic validation of the method. Circulation 1977;55:613-8.
29. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I *et al.* Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 1986;57:450-8.
30. Wyatt HL, Meerbaum S, Heng MK, Gueret P, Corday E. Cross sectional echocardiography III. Analysis of mathematic models for quantifying volume of symmetric and asymmetric left ventricular. Am Heart J 1980;100:821-8.
31. Corrao S, Parrinello G, Arnone S, Indovina A, Scaglione R, Licata G. Influence of obesity on the echocardiographic evaluation of left ventricular ejection fraction by area-length method: comparison with radionuclide angiography. J Cardiov Diagnos Proced 1993;11:127-34.
32. Corrao S, Paterna S, Arnone S, Costa R, Amato V, Amico G *et al.* Two-dimensional echocardiographic evaluation of left ventricular

ejection fraction by the ellipsoid single-plane algorithm: a reliable method for assessing low or very low ejection fraction values? Cardiology 1995;86:503-7.
33. Missri J. Clinical Doppler echocardiography. Spectral and color flow imaging. New York: Mc Graw-Hill information Services Company, 1990:28-42.
34. Corrao S, Scaglione R, Arnone S, Licata G. Left ventricular diastolic filling alterations in subjects with mitral valve prolapse: a Doppler echocardiographic study. Eur Heart J 1993;14:369-72.
35. Fujii J, Yazaki Y, Sawada H, Aizawa T, Watanabe H, Kato K. Non invasive assessment of left and right ventricular filling in myocardial infarction with a two-dimensional Doppler echocardiographic method. J Am Coll Cardiol 1985;5:1155-60.
36. Kendall MG, Stuart A. The advanced theory of statistics. New York: Hafner Publishing Company, 1973, vol 2.
37. Alexander JK. The heart and obesity. In: Hurst JW, Logue RB, Rackley CE, Schiant RC, Sonnenbiick EH, Wallace NK, editors. The heart. New York: McGraw Hill, 1982:1584-90.
38. Alpert MA, Terry BE, Lambert CR, Kelly DL, Panayiotou H, Yiukerji V *et al.* Factors influencing left ventricular systolic function in nonhypertensive morbidly obese patients, and effect of weight loss induced by gastroplasty. Am J Cardiol 1993;71:733-7.
39. Himeno E, Nishino K, Nakashima Y, Kuroiwa A, Ikeda M. Weight reduction regresses left ventricular mass regardiess of blood pressure level in obese subjects. Am Heart J 1996;131:313-9.
40. Labovitz AJ, Pearson AC. Evaluation of left ventricular function: clinical relevance and recent Doppler echocardiographic insights. Am Heart J 1987;114:336-51.
41. Thomas JD, Weyman AE. Echocardiographic Doppler evaluation of left ventricular diastolic function. Circulation 1991;84:977-90.