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Cardiovascular and adrenergic response to exercise in obese subjects

A. Salvadori, P. Fanari, P. Palmulli, E. Giacomotti, M. Arreghini, G. Bolla, G. Miserocchi, E. Longhini

In obese subjects a decreased work capacity has been described and abnormalities of left ventricular diastolic filling have been observed at rest. The aim of this study was to estimate the cardiovascular and adrenergic response of obese, otherwise healthy subjects to increasing work loads on a bicycle ergometer compared to normal subjects.

At first we examined 18 obese subjects (9 males) aged 17 to 42 years and mean body mass index (BMI) 40 kg/m² and 18 non-obese control subjects (9 males) aged 19 to 39 years and BMI 22 kg/m² who performed an incremental exercise test with steps of 20 W every four minutes up to exhaustion. Oxygen consumption ($\dot{V}O_2$), heart rate (HR), maximal peak of activity and ventilatory anaerobic threshold (AT) were measured, looking for differences of gender between the obese group and the control group. Afterwards, we studied 12 subjects (6 males) from both groups of control and obese subjects in which we also assessed plasma epinephrine (E), heart rate blood pressure product and CK-MB isoenzyme. On a separate occasion, cardiac output was measured in these two groups of 12 subjects at four increasing steps below ventilatory anaerobic threshold (AT) using a CO₂ rebreathing method.

Among the obese as well as the control subjects, males demonstrated a higher work capacity due to a higher AT. The similar slope of $\dot{V}O_2$ vs. watts in all cases, indicated an identical net mechanical efficiency between male and female subjects of the two groups.

Considered as a whole, obese subjects of the analysed subgroups had, for the same work load, a similar cardiac output, a greater oxygen consumption, a greater arterio-venous oxygen difference and a smaller stroke volume. The estimated ratio of blood flow to fat free body mass was higher at any submaximal work load in non-obese compared to obese subjects. The increase of heart rate during incremental exercise was lower in the obese group and well correlated with plasma E levels. The heart rate-systolic blood pressure product, representing an indirect index of myocardial oxygen consumption, was higher, at any work load in obese compared to control subjects. The creatinphosphokinase cardiac isoenzyme (CK-MB) plasma concentrations after 5 min of recovery was significantly higher in obese subjects compared to controls.

In summary, the data indicate that obese subjects have a decreased working capacity compared to non-obese people with a peculiar adrenergic answer to progressive physical exercise. In the absence of medical problems, they may be regarded as less fit individuals, probably with a reduced cardiac efficiency at heavier workloads. *J Clin Basic Cardiol* 1999; 2: 229–36.

Key Words: obesity, cardiac output, oxygen consumption, exercise, creatine kinase, epinephrine, anaerobic threshold

Both the ventilatory and cardiovascular systems are stressed during physical exercise and the ability to support adequately the increased metabolic rate and gas-exchange of contracting muscles during exercise reflects their efficiency. Obesity is a disorder that can limit physical activity because of the additional energy needed to move larger bodies [1]. The increased body mass requires a greater metabolic energy exchange both at rest and especially during physical exercise [1]. Obese subjects use a greater amount of O₂ to accomplish an equal external workload when compared to non-obese subjects [2]. Obesity usually exhibits lung function abnormalities like a decrease in compliance of the respiratory system [3] and a decrease of functional residual capacity [4]. In obese people there is an increase of cardiac work at rest, estimated at 40 to 190 per cent relative to that of subjects of ideal body weight [5]. It is well established that indexes of obesity, such as Body Mass Index (BMI), correlate with left ventricular mass, wall thickness and cavity dimension [6] although relatively few studies have been performed on diastolic or cardiac contractile function in obesity.

The aim of this study was to investigate the cardiovascular and adrenergic responses of obese subjects to increasing workloads during a cycle ergometric exercise and to look for differences, if any, between obese and non-obese males and females concerning work capacity and mechanical efficiency.

Methods

Total sample analysis

We studied 18 obese subjects and 18 control subjects (9 males and 9 females in each group), both groups being untrained and without cardio-respiratory disorders, all employed as administrative or teaching staff. Obesity was defined on the basis of BMI (kg/m²) > 25 [7]. The obese and control groups were matched for sex, age and height (see Table 1a and 1b). Exercise capacity was quantified by determining their maximum work rate, ventilatory anaerobic threshold (AT), and $\dot{V}O_2$ max defined as the $\dot{V}O_2$ averaged over the last minute of exercise.

The ergospirometric test was performed on a bicycle ergometer (Gould), at a pre-set pedalling rate (60 cycles/min) at least 3 hours after lunch in every one of the 36 subjects of the two groups. Subjects were studied at rest and during free pedalling lasting 4 min. Next, the ergometric test was started with an initial workload of 20 W, followed by subsequent steps of 20 W every 4 min until the subject could no longer maintain pedalling frequency. After exercise dropout, the subject was followed for up to 20 min during recovery, maintained in a sitting position (modified protocol of Sjöstrand) [8].

An ergospirometer (MMC Horizon™ System 4400TC; Sensor Medics) was used to record oxygen consumption ($\dot{V}O_2$),

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minute ventilation ($\dot{V}_E$) and end tidal O_2 and CO_2 pressures (PET_{O_2} and PET_{CO_2} respectively). The gases were sampled at the mouth by means of a 210 cm long heated tube (100 °C). A HP series 300 personal computer was connected to the equipment to store and analyse data.

Calibrations were performed prior to each test. For baseline condition, free pedalling and at each workload, we considered the mean data obtained during the last minute of registration.

We recorded heart rate and ECG signals by a Cardiovit AT-60 (Schiller) and oxyhaemoglobin saturation by means of a Radiometer percutaneous oxymeter. Blood haemoglobin was determined in all subjects.

The anaerobic threshold was determined by using the following criteria [9–11]:

1. inflection point on the $\dot{V}_E$ vs. $\dot{V}_{O_2}$ diagram;
2. point of increase in PET_{O_2} ;
3. point of increase in the ventilatory equivalent of O_2 ($\dot{V}_E/\dot{V}_{O_2}$) without a concomitant reduction of partial PET_{CO_2} .

Subgroup analysis

In a subgroup of 24 subjects (12 obese subjects [6 males] and 12 normal subjects [6 males] [Table 2]), we assessed fat and fat-free mass by means of a tetrapolar bioelectrical impedance method (BIA 101/S, Akem, Florence, Italy). Predicted maximum $\dot{V}_{O_2}$ (highest $\dot{V}_{O_2}$ attained during presumed maximal effort) was calculated in each subject using the formula suggested by Wasserman et al. [2].

Epinephrine determination

By means of a needle inserted into the antecubital vein connected to a saline solution, blood samples were collected at the end of each step of increasing work, to determine epinephrine (E) by High Performance Liquid Chromatography (HPLC) [12].

CK-MB Isoenzyme determination

CK-MB isoenzyme plasma concentration was determined from blood samples collected by means of a needle inserted into the antecubital vein at rest, at the highest workload and after 5 minutes recovery.

CK-MB was determined by an immunological method with starter reagent, using a specific antibody that inhibits CK-M subunits without the CK-B subunit being affected; thereafter, the remaining CK-B activity, corresponding to 50 % of total CK-MB activity, was determined by means of the activated CK N-acetylcysteine (NAC) activated method (Boehringer-Ingelheim). In our laboratory, the interassay CV for this test varies, with increasing serum concentrations, from 4.2 % to 0.7 % and the interassay CV from 2.0 % to 1.3 %.

Cardiac Output determination

The day after the ergometric test, we estimated cardiac output ($\dot{Q}$). We chose the following steps for a quadrangular protocol, each step lasting 4 minutes: rest, free pedalling, 40 and 70 W, the last workload being, as from previous determinations, below anaerobic threshold. We used a 20 s CO_2 rebreathing method, as described by Jones [13], that allows cardiac output determination during the last minute of each workload. In every subject we measured no significant increase of blood lactate (Accusport capillary blood lactate, Boehringer Mannheim) at each work rate compared to rest conditions, which meant the absence of an unbalance between its production and consumption.

We choose this method for ethical reasons and its reliability [14, 15]. Every subject, while pedalling at rest and at a

given workload, was connected, at the end of a normal expiration, to a bag containing 4 litres of a mixture of CO_2 (from 7 to 11 % with different workloads) in O_2 . Inspired $Pbag_{CO_2}$ and PET_{CO_2} were continuously recorded with an infrared analyser. A perfect plateau of both, indicating cessation of CO_2 exchange between mixed venous blood and alveolar gas was given by fluctuations in carbon dioxide tension less than 0.5 mmHg during a complete rebreathing cycle. When the plateau was not reached, we repeated the test with a different CO_2 concentration in the rebreathing bag (as previously indicated).

Arterial pressure for carbon dioxide (P_{aCO_2}) was estimated from corrected PET_{CO_2} according to the formula [13]:

$$P_{aCO_2} = 5.5 + 0.9 PET_{CO_2} - 0.0021 V_t$$

where V_t is tidal volume (ml).

Mixed venous carbon dioxide tension (P_{vCO_2}) was obtained from the rebreathing equilibrium plateau with a downstream correction [13]:

$$P_{vCO_2} = P_{bagCO_2} - (0.24 P_{bagCO_2} - 11)$$

where P_{bagCO_2} is the gas partial pressure in the rebreathing bag at the equilibrium plateau.

The partial pressures were converted into arterial and venous plasma concentrations according to the general equation (C_{CO_2} [ml.dl⁻¹] = 11.02 $P_{CO_2}^{0.396}$) where C_{CO_2} is the carbon dioxide content [13].

Finally cardiac output ($\dot{Q}$) was obtained by using the Fick formula:

$$\dot{Q} = \frac{\dot{V}_{CO_2}}{C_{vCO_2} - C_{aCO_2}}$$

where $C_{vCO_2} - C_{aCO_2}$ is the venous-arterial concentration difference for CO_2 .

The institutional ethics committee approved the investigation, and each volunteer gave his informed consent.

Data analysis

$\dot{V}_{O_2}$, heart rate, cardiac output values and CK-MB isoenzyme obtained at each step of the test were compared between groups by analysis of variance (ANOVA). Dunnett's method was used to determine the statistical difference of the above parameters between obese and non-obese subjects at each step of exercise [16]. A difference was considered statistically significant for $p < 0.05$. Values are expressed as mean $\pm$ SEM.

We used the least-squares criterion applying ANOVA to the regression model to calculate the straight-line regressions [17]. We finally compared the calculated straight-line regressions considering body mass as a dummy variable Z equal to 1 and 0 for obese and normal subjects respectively. The model is given by: $Y = \beta_0 + \beta_1 X + \beta_2 Z + \beta_3 XZ + E$, where Y and X are the two considered variables and Z is the dummy variable indicating normal or obese subjects. Based on this approach, we performed appropriate tests for coincidence, parallelism and equal intercepts [17].

Results

Total sample analysis

We report in Table 1a the mean anthropometric and functional data of the two groups, and in Table 1b the data segregated by sex.

The peak of exercise at exhaustion, when expressed as work rates, was not different between the two groups; AT was significantly lower in the obese subjects but at similar levels of oxygen consumption (Table 1a).

Weight and height were significantly different by sex in both groups, while BMI was significantly different between males and females only in the control group (Table 1b).

Considering the comparison between males and females, AT and the peak of exercise at exhaustion, when expressed as work rates, were different both in the non-obese and the obese

group with analogy. AT was at similar levels of oxygen consumption in males and females of both groups (Table 1b).

In Figure 1 and Figure 2 we represent the linear correlations between $\dot{V}O_2$ and watts and between heart rate and watts in normal and in obese male and female subjects. Figure 1 shows that with increasing workloads $\dot{V}O_2$ was constantly higher in the males than in females, with a significant difference in the normal group. The regression of HR vs. watts displays significantly similar higher slopes for females in both groups compared to males.

Table 1a. Anthropometric and functional data of the global sample

	Group		
	Non-obese subjects	Obese subjects	p Value ^a
No. of subjects	18	18	NS
Sex, M/F	9/9	9/9	NS
Age (years) ^b	27 ± 1	26 ± 2	NS
Weight (kg) ^b	66 ± 3	115 ± 4	< 0.001
Height (cm) ^b	171 ± 3	169 ± 2	NS
BMI (kg/m ²) ^b	22 ± 1	40 ± 1	< 0.001
Exhaustion (watts) ^b	147 ± 9	126 ± 8	NS
AT (watts) ^b	105 ± 7	78 ± 6	< 0.01
$\dot{V}O_2$ at AT (ml/min) ^b	1515 ± 90	1492 ± 51	NS

^a By two tailed analysis of variance.

^b Values are mean ± s.e.m.

Abbreviations: BMI = body mass index; AT = anaerobic threshold.

Subgroup analysis

Table 2 reports the anthropometric and functional data of the subgroups of the studied subjects. The expiratory reserve volume, the functional residual capacity, residual volume and total lung capacity were significantly decreased in the obese subjects. Pulmonary diffusing capacity for CO was in the normal range in both groups.

The oxyhaemoglobin saturation was within normal limits in obese and non-obese subjects at rest and did not decrease during physical exercise at the highest workloads. Blood haemoglobin contents were normal and similar between the two groups (14.3 ± 1.2 in control vs. 14.6 ± 1.6 [g/dl] in obese subjects).

Table 3 summarises the absolute values of oxygen consumption and heart rate (HR) for different work loads in the two groups. Oxygen consumption was significantly higher in obese subjects at all submaximal workloads, but peak values

Table 1b. Anthropometric and functional data segregated by sex

	Non-obese subjects		Obese subjects	
	Males	Females	Males	Females
No. of subjects	9	9	9	9
Age (years) ^a	28.3 ± 1.7 (20–39) ^b	26.5 ± 1.5 (23–36) ^b	23.7 ± 1.5 (18–32) ^b	28.0 ± 2.8 (19–42) ^b
Weight (kg) ^a	74.8 ± 2.4 (64–85) ^b	54.7 ± 1.4 (49–61) ^{b***}	122.9 ± 4.6 (106–152) ^b	106.5 ± 6.1 (82–130) ^{b*}
Height (cm) ^a	178.3 ± 3.2 (162–194) ^b	161.4 ± 1.6 (154–168) ^{b***}	175.2 ± 1.4 (170–181) ^b	161.2 ± 2.9 (150–175) ^{b***}
BMI (kg/m ²) ^a	23.6 ± 0.8 (20–25) ^b	21.5 ± 0.5 (19–24) ^{b*}	40.1 ± 1.5 (36–49) ^b	40.8 ± 1.4 (35–47) ^b
Exhaustion (watt) ^a	166 ± 13	122 ± 7*	147 ± 10	102 ± 6**
AT (watt) ^a	121 ± 9	87 ± 9*	91 ± 8	61 ± 6*
$\dot{V}O_2$ at AT (ml/min) ^a	1634 ± 133	1360 ± 93	1550 ± 67	1400 ± 69

* = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$, by two tailed analysis of variance males vs. females.

^a Values are mean ± s.e.m.

^b Absolute range values for anthropometric data.

Table 2. Anthropometric and lung function data of the subgroups of subjects

	Group		
	Non-obese subjects	Obese subjects	p Value ^a
No. of subjects	12	12	NS
Sex, M/F	6/6	6/6	NS
Age (years) ^b	27 ± 1.6 (19–39) ^c	26 ± 2.4 (17–42) ^c	NS
Weight (kg) ^b	64 ± 3.2 (49–85) ^c	111 ± 8.6 (91–144) ^c	< 0.001
Height (cm) ^b	169 ± 3 (154–194) ^c	166 ± 2 (150–180) ^c	NS
BMI (kg/m ²) ^b	22 ± 1 (19–25) ^c	40 ± 1 (35–46) ^c	< 0.001
Fat-free mass (kg) ^b	50 ± 4 (33–70) ^c	71 ± 4 (54–83) ^c	< 0.01
% Fat-free mass (%) ^b	74 ± 4	64 ± 2	NS
VC (L) ^b	5.6 ± 0.4 (120 %) ^d	4.7 ± 0.3 (107 %) ^d	NS
ERV (L)(BTPS) ^b	1.8 ± 0.4 (95 %) ^d	0.9 ± 9.2 (104 %) ^d	< 0.01
FRC (L)(BTPS) ^b	3.8 ± 0.3 (114 %) ^d	2.1 ± 0.1 (124 %) ^d	< 0.001
RV (L)(BTPS) ^b	2.1 ± 0.2 (138 %) ^d	1.2 ± 0.2 (154 %) ^d	< 0.05
TLC (L)(BTPS) ^b	7.8 ± 0.7 (122 %) ^d	5.7 ± 0.3 (107 %) ^d	< 0.05
Dl _{CO} (mL/min/mmHg) STPD ^b	44.7 ± 9.4 (142 %) ^d	33.9 ± 2.6 (121 %) ^d	NS
HbO ₂ Sat (%) ^b	96 ± 1	95 ± 1	NS
Max. $\dot{V}O_2$ (% of predicted) ^b	93 ± 2	77 ± 4	NS

^a By two tailed analysis of variance.

^b Values are mean ± s.e.m.

^c Absolute range values for anthropometric data.

^d Percent lung function data.

Abbreviations: BMI = body mass index; VC = vital capacity; ERV = expiratory reserve volume; FRC = functional residual capacity; RV = residual volume; TLC = total lung capacity; Dl_{CO} = diffusing capacity of lung for CO; HbO₂ Sat = O₂ saturation of haemoglobin in arterialised blood; Max. $\dot{V}O_2$ = Predicted maximum $\dot{V}O_2$ as from Wasserman et al. [20].

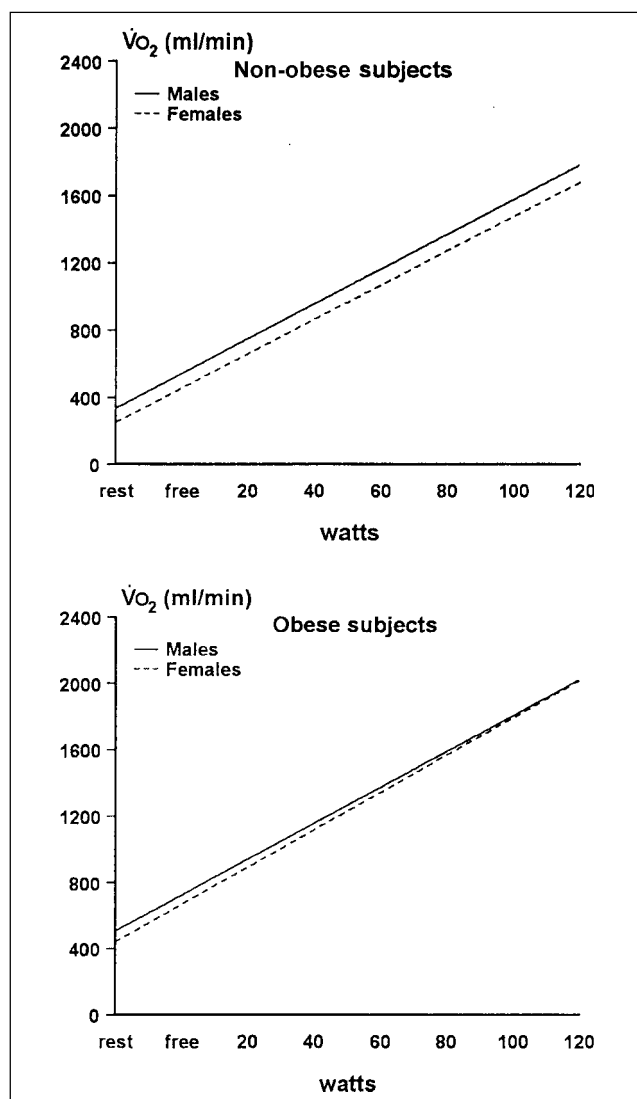


Figure 1. Oxygen consumption ($\dot{V}O_2$) vs. watts relationship in non-obese and obese males and females. The regression lines were: $\dot{V}O_2 = 363.6 + 11.4 \text{ watt} + 91.4Z_2$ ($R^2: 0.95$; F: 1420; MSE: 10445) in the control group, and $\dot{V}O_2 = 615.3 + 12 \text{ watt}$ ($R^2: 0.65$; F: 93; MSE: 247.6) in the obese group, with a dummy variable $Z_2 = 1$ for males and 0 for females in the regression line of the normal group because the two regression lines are parallel, but not coincident ($p < 0.001$).

of oxygen uptake at exhaustion did not differ between groups. Table 3 also reports the maximum oxygen uptake ($\dot{V}O_{2\text{max}}$) calculated as suggested by Wasserman [2] that is higher in obese compared to control people. When related to body mass, maximum aerobic power was obviously larger in non-obese subjects compared to obese subjects (35 and 25 ml/min/kg, in non-obese and obese subjects, respectively). $\dot{V}O_2$ at exhaustion was 93 and 77 % of $\dot{V}O_{2\text{max}}$ in control and obese subjects respectively.

Anaerobic threshold was at similar levels of oxygen consumption (1520 ± 93 ml/min in obese subjects vs. 1710 ± 153 ml/min in control subjects; $p = \text{NS}$), but was reached at a significantly lower workload in obese subjects (79 ± 7 W vs. 110 ± 10 W; $p < 0.05$).

Heart rate was significantly higher in obese subjects at rest, at free pedalling and up to a work rate of 40 W. At exhaustion, however, it was significantly lower than in controls (Table 3).

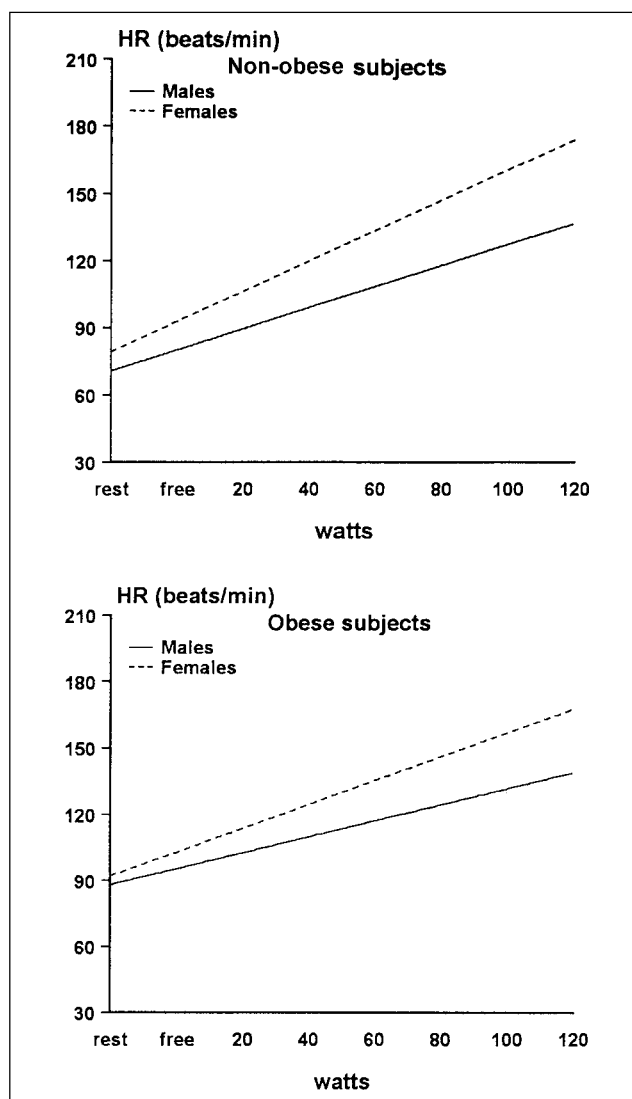


Figure 2. Heart rate (HR) vs. watt relationship in non-obese and obese males and females. The regression lines were: $HR = 90.7 + 0.7 \text{ watt} - 14.2Z_2 - 0.2 \text{ watt}Z_2$ ($R^2: 0.8$; F: 205; MSE: 248) in the control group, and $HR = 98 + 0.6 \text{ watt} - 5.8Z_2 - 0.2 \text{ watt}Z_2$ ($R^2: 0.8$; F: 180; MSE: 145) in the obese group, with a dummy variable $Z_2 = 1$ for males and 0 for females because the two regression lines have significantly different slopes ($P < 0.001$).

No alteration of ECG signals, in particular of the ST segment, was monitored in any subject during and after the ergometric test.

The correlation between heart rate and $\dot{V}O_2$ was linear in both groups (Fig. 3) and comparing the two straight lines they had statistically different slopes ($p < 0.05$). Indeed, the single multiple regression model was: $HR = 66.576 + 0.05 \dot{V}O_2 + 11.44Z + 0.01 \dot{V}O_2Z$ ($R^2: 0.65$; F: 93; MSE: 247.6), with a dummy variable $Z = 1$ for the obese subjects and 0 for the control subjects. These regressions could be used to derive $\dot{V}O_{2\text{max}}$ extrapolating to HRmax; the corresponding values (2680 and 3190 ml/min respectively in controls and obese subjects, reported in Table 3) compare reasonably well with those obtained as suggested by Wasserman [2] (2290 and 2770 ml/min respectively in controls and obese subjects). Introducing the variable sex in this equation ($Z_2 = 1$ for males and $Z_2 = 0$ for females) the model fitted better ($R^2: 0.79$; F: 116.3; MSE: 145.3) and the single regression model was:

Table 3. Oxygen consumption ($\dot{V}O_2$) and heart rate of non-obese and obese subjects during exercise testing (modified triangular protocol of Sjöstrand) (mean $\pm$ s.e.m.)

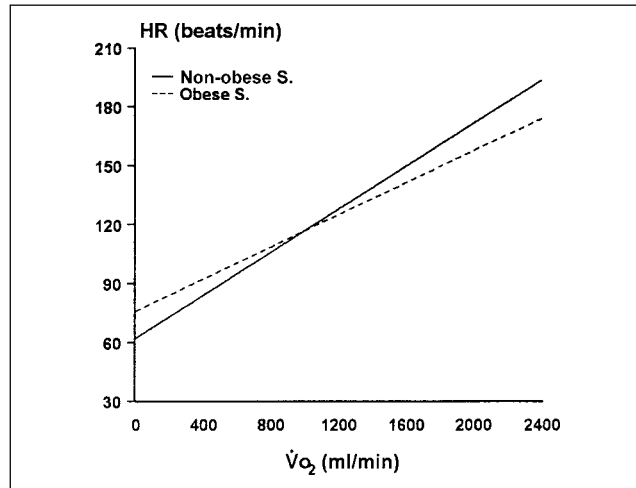
Workload	$\dot{V}O_2$ (ml/min)		Heart rate (beats/min)	
	Non-obese subjects	Obese subjects	Non-obese subjects	Obese subjects
Rest (n = 12,12) ^a	350 $\pm$ 19	450 $\pm$ 33	76 $\pm$ 2	93 $\pm$ 3**
Free pedalling (n = 12,12) ^a	490 $\pm$ 40	820 $\pm$ 36**	86 $\pm$ 3	106 $\pm$ 3**
20 W (n = 12,12) ^a	670 $\pm$ 28	980 $\pm$ 43**	97 $\pm$ 4	112 $\pm$ 3*
40 W (n = 12,12) ^a	820 $\pm$ 32	1090 $\pm$ 40**	105 $\pm$ 5	120 $\pm$ 4*
60 W (n = 12,12) ^a	1060 $\pm$ 26	1350 $\pm$ 44**	122 $\pm$ 5	130 $\pm$ 5
80 W (n = 12,12) ^a	1260 $\pm$ 29	1580 $\pm$ 47**	133 $\pm$ 6	138 $\pm$ 4
100 W (n = 12,11) ^a	1530 $\pm$ 35	1800 $\pm$ 46**	148 $\pm$ 6	144 $\pm$ 5
120 W (n = 9,7) ^a	1770 $\pm$ 57	1980 $\pm$ 40*	153 $\pm$ 5	150 $\pm$ 4
Peak values at exhaustion (n = 12,12) ^a	2020 $\pm$ 175	2070 $\pm$ 116	171 $\pm$ 3	157 $\pm$ 4*
Max. values calculated from Wassermann [20]	2290 $\pm$ 210	2770 $\pm$ 225.3	189 $\pm$ 2	194 $\pm$ 1
Max. values predicted from Fig. 1	2680 $\pm$ 250	3190 $\pm$ 280	195	192
AT (n = 11,11) ^a	1710 $\pm$ 153	1520 $\pm$ 93	149 $\pm$ 4	138 $\pm$ 4*

^a Number of control and obese subjects.* $p < 0.05$; ** $p < 0.01$; Two-tailed analysis of variance and Dunnett's method.

Abbreviation: AT = Anaerobic threshold.

Table 4. Cardiac output ($\dot{Q}$) and $\dot{Q}$ /fat-free mass of non-obese and obese males during exercise testing (quadrangular protocol) (Values are mean $\pm$ s.e.m.)

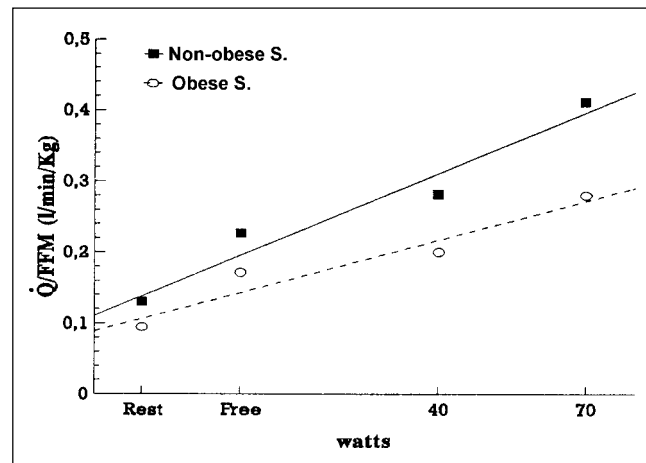
Work load	$\dot{Q}$ (ml/min)		$\dot{Q}$ /fat-free mass (ml/min/kg)	
	Non-obese subjects	Obese subjects	Non-obese subjects	Obese subjects
Rest	6.1 $\pm$ 0.9	6.9 $\pm$ 0.7	0.129 $\pm$ 0.01	0.093 $\pm$ 0.01
Free pedalling	11.0 $\pm$ 0.9	11.7 $\pm$ 0.9	0.224 $\pm$ 0.02	0.170 $\pm$ 0.02
40 W	13.7 $\pm$ 0.9	13.7 $\pm$ 0.6	0.281 $\pm$ 0.02	0.199 $\pm$ 0.01*
70 W	18.3 $\pm$ 0.9	17.5 $\pm$ 0.9	0.379 $\pm$ 0.03	0.261 $\pm$ 0.02*

* $p < 0.05$; Two-tailed analysis of variance and Dunnett's method.**Figure 3.** Heart rate (HR) vs. oxygen consumption ($\dot{V}O_2$) relationship in non-obese and obese subjects. The regression was: $HR = 66.576 + 0.05 \dot{V}O_2 + 11.44Z + 0.01 \dot{V}O_2Z$ (R^2 : 0.65, F: 93; MSE: 247.6), with a dummy variable $Z = 1$ for the obese subjects and 0 for the non-obese. The two straight lines have statistically different slopes ($p < 0.05$).

$$HR = 65.15 + 0.06 \dot{V}O_2 + 12.87Z - 4.54Z_2 - 0.01 \dot{V}O_2Z - 0.01 \dot{V}O_2Z_2$$

The cardiac output was similar in obese and control subjects for the same workload (Table 4). Table 4 also reports the ratio of cardiac output to fat free mass that becomes significantly lower in obese compared to control subjects at 40 and 70 W.

Figure 4 shows that, with increasing workloads, blood flow into the fat-free component increases more in non-obese compared to obese subjects ($p < 0.05$). The single multiple regression model was: $\dot{Q}/FFM = 0.169 + 0.003 \text{ watts} - 0.045Z$

**Figure 4.** Blood flow per unit body fat-free mass ($\dot{Q}/FFM$) plotted vs. mechanical power output in control and obese subjects. The regression was: $\dot{Q}/FFM = 0.169 + 0.003 \text{ watt} - 0.045Z - 0.001 \text{ watt}Z$ (R^2 : 0.69; F: 53; MSE: 0.004), with a dummy variable $Z = 1$ for the obese subjects and 0 for the non-obese subjects. The regression for obese subjects displays a significantly lower slope compared to controls ($p < 0.05$).

- 0.001 wattsZ, with a dummy variable $Z = 1$ for the obese subjects and 0 for the control subjects.

Figure 5 shows that the $\dot{V}O_2$ to fat-free mass ratio increases with increasing workload, but to a greater extent in normal compared to obese subjects; furthermore, the maximum value of this ratio is significantly higher in non-obese compared to obese subjects.

Figure 6 is a plot of cardiac output ($\dot{Q}$) vs. oxygen uptake ($\dot{V}O_2$); the figure also reports iso-arterio-venous (a-v $\dot{D}O_2$) and iso-workload lines. As it can be seen, in non-obese subjects an increase in oxygen consumption occurs together with an

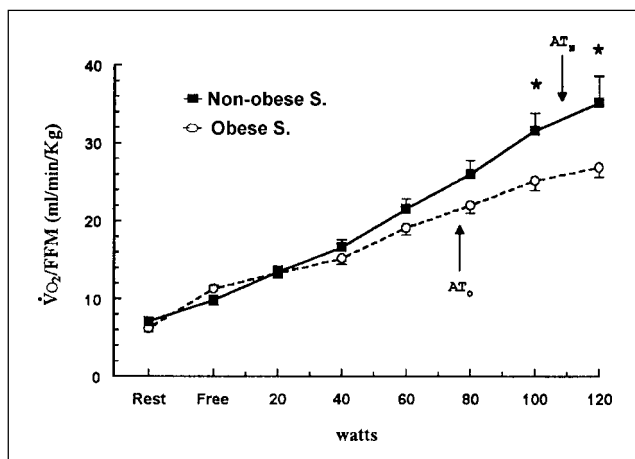


Figure 5. Relationship between oxygen consumption, normalised for fat free mass ($\dot{V}O_2/FFM$) vs. mechanical power output. AT_N and AT_O refer to anaerobic threshold for non-obese and obese subjects. * = $p < 0.05$

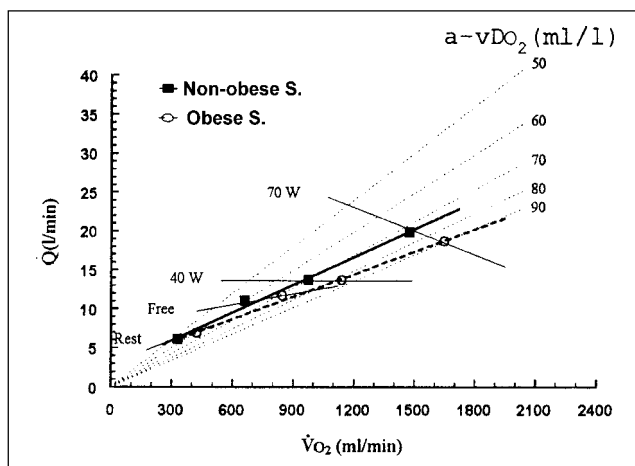


Figure 6. Cardiac output ($\dot{Q}$) vs. oxygen consumption ($\dot{V}O_2$) in non-obese and obese subjects with increasing workload. Also shown are iso-workload and iso-arterio-venous oxygen difference lines ($a-vDO_2$). The regression was: $\dot{Q} = 2.414 + 0.01 \dot{V}O_2 + 0.494Z - 0.0021 \dot{V}O_2Z$ ($R^2: 0.83$; $F: 133$; $MSE: 4.5$), with a dummy variable $Z = 1$ for the obese and 0 for the non-obese subjects. The regression for obese subjects displays a significantly lower slope compared to controls ($p < 0.05$).

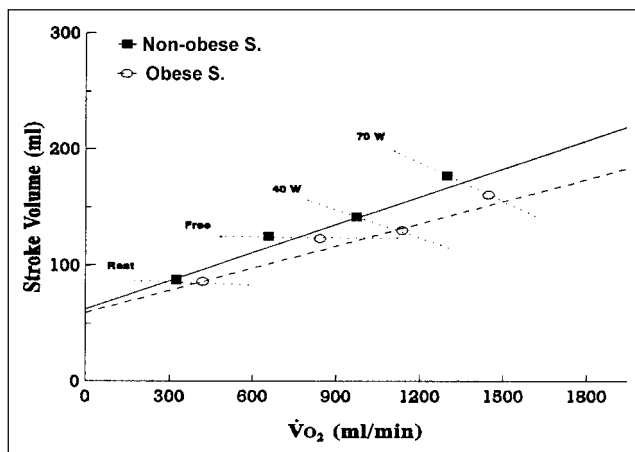


Figure 7. Relationship of stroke volume vs. oxygen consumption ($\dot{V}O_2$) in non-obese and obese subjects. The graph reports iso-workload lines. The regression was: $\text{Stroke Volume} = 0.062 + 0.001 \dot{V}O_2 - 0.003Z$ ($R^2: 0.53$; $F: 31$; $MSE: 0.001$), with a dummy variable $Z = 1$ for the obese subjects and 0 for the non-obese subjects. The relationship relative to obese subjects displays statistically similar slopes and a lower intercept compared to controls ($p < 0.01$).

increase in arterio-venous oxygen difference. The regression for obese subjects displays a significantly lower slope compared to controls ($p < 0.05$); in fact, obese subjects rely on a greater arterio-venous oxygen difference for the same oxygen consumption and, in addition, have a greater oxygen consumption for the same workload. The single multiple regression model was: $\dot{Q} = 2.414 + 0.01 \dot{V}O_2 + 0.494Z - 0.0021 \dot{V}O_2Z$, with a dummy variable $Z = 1$ for the obese subjects and 0 for the non-obese subjects.

Figure 7 shows a plot of stroke volume vs. oxygen uptake and the relationship relative to obese subjects displays statistically similar slopes and a lower intercept compared to controls ($p < 0.01$). The single multiple regression model was: $\text{Stroke volume} = 0.062 + 0.001 \dot{V}O_2 - 0.003Z$, with a dummy variable $Z = 1$ for the obese subjects and 0 for the non-obese subjects. It appears that, for the same oxygen consumption, stroke volume is lower in obese compared to controls: this is in accordance with a higher heart rate and a greater arterio-venous oxygen difference. Iso-workload lines indicate that, for a given load, obese subjects have a higher $\dot{V}O_2$ and a smaller stroke volume.

Systolic and diastolic blood pressures increased during exercise both in non-obese and obese subjects, with no significant difference between the two groups; mean values at rest (mmHg) were 116/77 in non-obese subjects and 120/84 in obese subjects. The corresponding values at exhaustion were 153/90 and 155/95 in control and obese subjects, respectively.

An indirect measure of myocardial oxygen consumption is given by the heart rate systolic blood pressure product (HRP) [18]. Figure 8A shows that, at any workload, HRP is higher in obese compared to non-obese people up to maximum workload. The ratio of HRP to $\dot{V}O_2$ decreases with increasing workload (Fig. 8B), due to the fact that with increasing power a larger proportion of total oxygen consumption is due to working muscles: yet this decrease appears markedly larger in obese compared to control subjects.

In Figure 9A mean plasma levels of epinephrine during the exercise tended to be higher at low work rates and were clearly lower at maximal exercise in the obese subjects when compared to controls. This behaviour is substantially in agreement with previous data from Gustafson [19]. In Figure 9B the plots of epinephrine vs. HR display a linear correlation in the obese group and an exponential one in the controls.

In Table 5 we report CK-MB plasma concentration and its confidence intervals. It was higher, though not significantly, in obese relative to non-obese, at rest and at peak workload; however, during recovery, CK-MB plasma concentration increased in obese subjects and decreased in non-obese subjects, the difference being significant [20].

Discussion

In this study we describe the cardiovascular and adrenergic response of obese, otherwise healthy, subjects to increasing workloads compared to the response of normal control subjects matched for age and sex.

We used the cycle ergometer test because it has the advantage that the work output performed by the subject is known and the differences in constitution probably weakened; in this condition more information is learned about cardiovascular function and gas exchange [2].

We assessed fat and fat-free mass by means of a tetrapolar bioelectrical impedance method to try to minimise differences in absolute values of some functional parameters. This method is based on the principle that the impedance of a geometrical system is related to conductor length and configuration, to its

cross sectional area, and to the signal frequency [21]. Any indirect method of assessing human body composition results in error of prediction. The impedance method implies an error of 2.7 % [21] that compares well with densitometry, the traditional reference method for assessment of body composition whose reported error is 2.5 % [22].

Obese and normal males appeared to have a greater working capacity due to the higher AT when compared to normal and obese females and tended to consume more oxygen at similar external workloads, probably due to a larger muscular mass. The increase in $\dot{V}O_2$ was the same between non-obese and obese males and females, as reflected by the same slope of the plot of $\dot{V}O_2$ vs. watts. At a first glance, this seems to indicate that the net mechanical efficiency (watts/ $\dot{V}O_2 - \dot{V}O_2$ free wheeling) between normal males and females, as well as between obese males and females, is virtually identical [23], while the gross mechanical efficiency (watts/ $\dot{V}O_2$) tends to be less in both non-obese and obese males [24, 25].

For any level of submaximal workload, HR was greater both in non-obese and obese females, probably depending on differences in muscular mass, haemoglobin content [26], heart size and levels of conditioning [27].

Considering the subgroups of obese and non-obese subjects on which we performed determinations of cardiac output, plasma epinephrine and CK-MB, we could not analyse for sex differences, if any, because of the relative low number of subjects. Nevertheless, we think that a comparison between obese and non-obese subjects as a whole may be appropriate in view of the above-listed analogous differences for sex.

Table 5. Myocardial creatine kinase isoenzyme (CK-MB) plasma concentration in non-obese and obese subjects in basal condition, at peak work rate and at 5 min during the post exercise recovery period

	Group		
	Non-obese subjects	Obese subjects	p Value ^a
Rest ^b	6.6 (4.8–8.4) ^c	8.2 (5.9–10.5) ^c	NS
Peak values at exhaustion ^b	6.9 (5.4–8.5) ^c	9.5 (7.0–12.0) ^c	NS
Min. 5 recovery ^b	6.2 (4.4–7.9) ^c	10.2 (6.9–13.5) ^c	< 0.05

^a By two tailed analysis of variance.

^b Values are mean

^c 95 % CI.

Maximal aerobic power was slightly higher in obese compared to normal people (Table 3); however, despite this advantage, obese subjects were at a marked disadvantage relative to controls in performing work for a series of reasons. First, the maximal aerobic power normalised per body mass is obviously lower in obese compared to normal subjects. Next, it appears that in obese subjects, the increase in heart rate is less

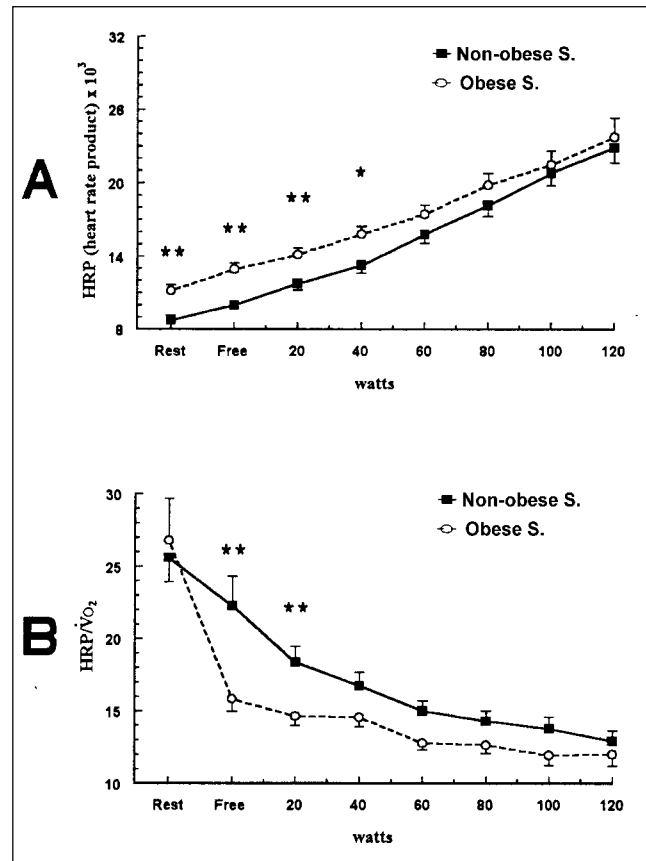


Figure 8A. Heart rate systolic pressure product (HRP) plotted vs. mechanical power output in control and obese subjects. **B.** Ratio of heart rate systolic pressure product to oxygen consumption (HRP/ $\dot{V}O_2$) plotted vs. mechanical power.

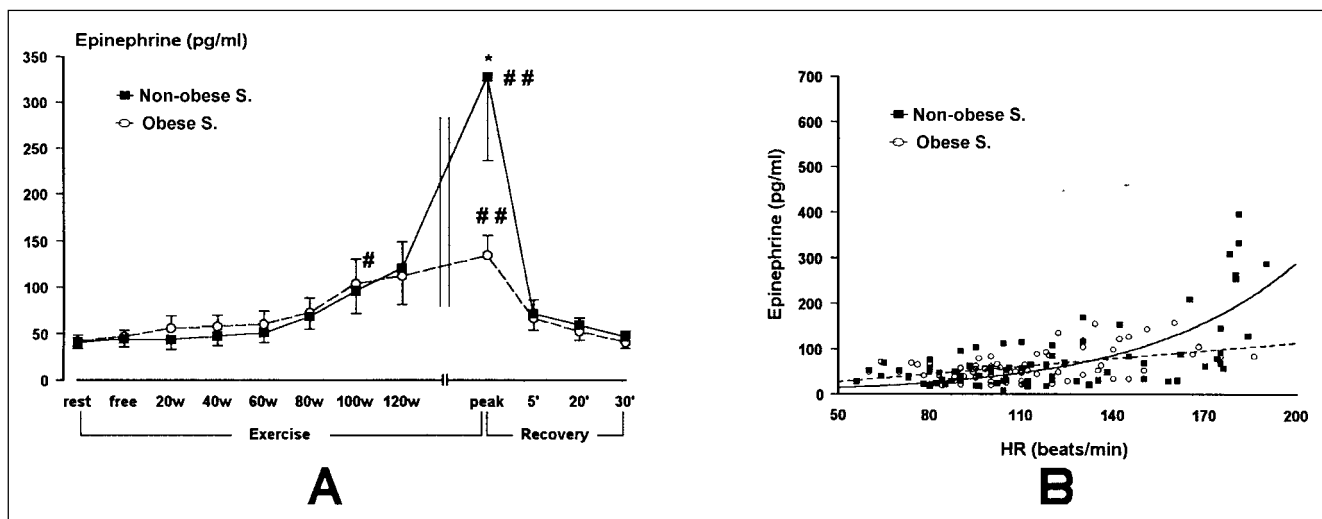


Figure 9A. Increments of epinephrine during progressive workloads. * = $p < 0.05$ normal vs. obese subjects; # = $p < 0.05$ exercise vs. rest values; ## = $p < 0.01$ exercise vs. rest values. **9B.** Plots of epinephrine vs. HR in non-obese and obese subjects. The regression was exponential for the non-obese subjects: $E = \exp(1.646 + 0.01 \text{ HR})$ ($R^2: 0.49$; $F: 36$; $MSE: 0.4$) and linear for the obese subjects: $E = -2.11 + 0.581 \text{ HR}$ ($R^2: 0.23$; $F: 22$; $MSE: 900$).

than that observed in non-obese subjects, for two reasons: in obese subjects, basal heart rate is higher than in controls and furthermore, the maximal heart rate attained is lower than in controls.

In general, the relationship between HR and oxygen uptake is linear, and its slope increases as the groups of muscle involved become progressively smaller (Fig. 3). These facts, already described [26, 28, 29], may be in agreement with the plot of HR in our obese subjects, together with their peculiar adrenergic response to exercise (Fig. 9A).

The unfavourable situation of muscle perfusion in obese subjects, compared to controls, can be appreciated by partitioning total cardiac output into the fat-free and fat components (Table 4, Fig. 4). Although it is true that during exercise there is an increase in blood flow to exercising muscles, this should occur to a lesser extent in obese subjects compared to control subjects as in the former a greater proportion of blood flow should be directed to the skin to enhance heat dissipation. Therefore the difference in blood flow per unit fat-free body mass ought to be larger than that shown in Figure 4.

A smaller $\dot{V}O_2$ to fat-free mass ratio for a given workload in obese subjects (Fig. 5) indicates a greater contribution of the anaerobic processes to the energy yield: this is in line with the fact that the anaerobic threshold was reached at a lower workload in obese compared to non-obese subjects. The last comment is also consistent with the finding of a lower cardiac output to fat free mass ratio (Fig. 4) and of a greater arterio-venous oxygen difference for a given workload (Fig. 6) in the obese group.

Obese subjects displayed less economy of exercise as they had a greater oxygen consumption for the same external power output (Fig. 6). This difference could reflect their unfavourable biomechanics related to the larger body mass. Actually, this unfavourable situation can worsen with increasing complexity of exercise, such as walking or jogging. Figure 6 also shows that, for a given oxygen uptake, arterio-venous difference was greater in obese compared to non-obese subjects. Furthermore, for any value of oxygen consumption, stroke volume was lower in obese subjects (Fig. 7).

A less favourable situation in obese subjects also occurs for the heart as suggested by data of Figures 8A and B. In fact, for any workload, the HRP, a representative index of myocardial oxygen consumption, is higher in obese compared to non-obese subjects (Fig. 8A); furthermore, the HRP to total $\dot{V}O_2$ ratio (expressing the ratio of heart rate to total body oxygen consumption) is smaller in the obese group (Fig. 8B). The greater load imposed on cardiac muscle is in line with the finding of a greater concentration in CK-MB, and in particular with an increase of this enzyme during post-exercise recovery (Table 5).

In general, untrained obese young subjects have a maximal sustainable working capacity that does not differ significantly from that of untrained non-obese subjects. Nevertheless, obese subjects appear to have a decreased working capacity compared with non-obese subjects.

Obesity is considered in literature to be a type of volume-overload state with left ventricular hypertrophy [6]. Significant abnormalities of left ventricular diastolic filling have been observed at rest in 50 % of asymptomatic morbidity of obese subjects compared with normal controls by pulse Doppler echocardiography. These abnormalities could not be attributed to abnormal systolic function or other conditions known to impair diastolic filling and may antedate a contractile impairment, representing a subclinical form of cardiomyopathy in the obese subjects [30].

Based on the present data, when no altered heart conditions can be detected, the obese subject ought to be regarded

as a less fit individual compared to normal, in terms of cardiovascular function during physical exercise, as much as a normal subject compared to a physically fit subject; moreover it has the disadvantage of a larger mass to be moved.

On the other hand, the lower slope in the linear correlations of cardiac output vs. oxygen uptake, as well as the reduced maximal heart rate at exhaustion together with a lower adrenergic answer to physical stress may be in line with a reduced cardiac efficiency while proceeding to heavier workloads in obese subjects.

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