Exercise and weight control in sedentary overweight men: effects on clinic and ambulatory blood pressure

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Objective To examine whether restriction of caloric intake and exercise of vigorous intensity can independently and additively influence clinic and ambulatory blood pressures in sedentary overweight men.

Design Sixty subjects aged 20–50 years were randomly allocated either to continue their normal caloric intake or to restrict it by 4186–6279 kJ/day, with 15% provided by protein, 30% by fat and 55% by carbohydrate, for 16 weeks. Within each of these groups subjects were further randomly allocated either to a control light intensity programme of exercise or to a vigorous intensity programme of exercise for 30 min three times a week. The light exercise group performed stationary cycling against no resistance, flexibility exercises and slow walking, The vigorous intensity group cycled on an ergometer at 60–70% of maximum their workload.

Results Fifty-one subjects completed the study. Their maximal oxygen uptake was increased by approximately 24% with vigorous exercise but did not change with light exercise. Caloric intake restriction led to a significant loss of body mass of 9.5 kg (95% confidence interval 7.6–11.3), whereas vigorous exercise had no effect. Restriction of caloric intake reduced supine clinic systolic and diastolic blood pressures significantly by 5.6 (2.3–8.9) and 2.4 mmHg (0.4–4.2), respectively. Relative to the control light exercise group, exercise of vigorous intensity exercise had no significant effect on clinic blood pressure. In contrast, time series analysis revealed that both caloric intake restriction and vigorous exercise were associated with lower daytime ambulatory systolic blood pressure, the reduction in systolic blood pressure being sustained throughout the 24 h period when vigorous exercise and caloric intake restriction were combined.

Conclusion Compared with the effects of caloric intake restriction, the effects of a vigorous exercise programme on blood pressure are inconsistent, there being no influence on clinic blood pressure but a reduction in daytime ambulatory blood pressure. However, when combined with caloric intake restriction, regular vigorous exercise exhibits a synergistic effect in reducing ambulatory blood pressure throughout a 24 h period.

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Introduction

The extent to which a subject is overweight is a significant and independent predictor of the level of blood pressure [1]. There is consistent evidence that weight loss by caloric intake restriction will lower blood pressure in the overweight [2], in hypertensives [3] and in normotensives [4,5]. The level of physical activity [6] or physical fitness [7] is also a significant predictor of blood pressure, but whether exercise without associated weight change can independently reduce blood pressure is controversial; some well-controlled studies in hypertensive [8,9] and normotensive subjects [10–12] have demonstrated falls in resting blood pressure with exercise, independent of weight loss, whereas others have not [13–15].

Fortmann *et al.* [4] reported that weight loss caused by moderate exercise reduced ambulatory, but not clinic, blood pressure in normotensive overweight men, with the reduction in blood pressure similar in magnitude to that found with weight loss achieved by caloric intake restriction. However, although this study was interpreted as demonstrating that exercise confers no unique benefit on blood pressure beyond the effect of caloric intake restriction alone, the combined effects of an exercise regimen and caloric intake restriction were not assessed. Since this original report [4], several studies have utilized ambulatory blood pressure monitoring (ABPM) to examine further the effects of exercise on blood pressure both in hypertensives [13,16–19] and in normotensives [20], with varied results. One study [20] observed falls in daytime but not in night-time diastolic blood pressure, whereas another showed reductions in daytime systolic blood pressure only [16]. Somers *et al.* [18] reported a reduction in waking blood pressure but no change in night-time blood pressure. Marceau *et al.* [19] also reported day–night differences in the effects of exercise on ambulatory blood pressure, but these were linked to the intensity of the exercise, with lower intensity exercise having its predominant effect on daytime blood pressure whereas higher intensity exercise reduced blood pressure only during the evening and sleeping hours. Others found no change in ambulatory blood pressure with exercise training of light or vigorous intensity [13,14,17].

All of these studies examined the mean 24 h blood pressure or the mean blood pressure for a specified period, such as mean daytime or night-time measurements. However, the use of summary statistics leads to a loss of information that can be overcome by a modelling approach with time series analysis (TSA), which is now feasible in analysing ABPM data [21]. Valid interpretation of such models requires that underlying statistical assumptions be fulfilled and sophisticated software such as Microfit [22] is now available for this purpose. Utilizing this approach, we assessed the effects of 16 weeks of vigorous exercise training, caloric intake restriction, or both, on the ambulatory blood pressure, clinic blood pressure and acute blood pressure response to exercise of sedentary overweight subjects.

By employing a two-way factorial design this study was able to assess the independent and combined effects of these two lifestyle modalities. The inclusion of a control light exercise group allowed us to minimize co-intervention bias and we carefully controlled for other potential confounders such as diet, alcohol consumption and salt intake, a feature not found in most exercise training studies.

Methods

Subjects

Non-smoking, overweight sedentary men aged 20–50 years were recruited in response to newspaper, radio and television advertisements. A total of 500 men were interviewed by telephone to assess whether they satisfied the initial criteria: alcohol consumption < 210 ml/week, body weight in the range 120–160% ideal weight for that man's height with no substantial weight loss (> 10 kg) in the preceding 12 months, a body mass index (BMI) > 25 kg/m^2, not receiving antihypertensive drugs, no history of myocardial infarction, stroke, coronary bypass surgery, renal or hepatic disease, diabetes mellitus or asthma, no musculoskeletal injury that would preclude exercise and no current treatment with non-steroidal anti-inflammatory drugs. A man was defined as sedentary if he had undergone fewer than two 30 min sessions of vigorous exercise a week during the previous 6 months.

Two hundred and sixty subjects who satisfied the initial criteria attended a screening visit, whereupon they completed a medical history and lifestyle questionnaire that further ascertained details of activity levels and alcohol consumption. Their blood pressure was measured using a Dinamap 1846SX (Critikon Inc., Tampa, Florida, USA) semi-automatic oscillometric recorder for 20 min with readings at 2 min intervals on two occasions 1 week apart. If the mean of these two blood pressures were within the range 130–160 mmHg systolic and 80–110 mmHg diastolic, the subject underwent a full medical examination, routine blood tests and a 12-lead resting electrocardiogram. Sixty subjects who satisfied all of the entry criteria participated in the study. The study protocol was approved by the University of Western Australia Committee for Human Rights and all of the subjects gave their written informed consent to participate.

Protocol

A 4-week run-in period included familiarization with blood pressure measurement and the fitness test. At the end of this time, during a 2-week baseline period, assessments were made of clinic blood pressure, 24 h ambulatory blood pressure, fitness, exercise blood pressure at 140 W on a bicycle ergometer and body weight. A health and lifestyle questionnaire that included the Spielberger Anxiety Scale Inventory [23] and the Profile of Mood State (POMS) Inventory [24] to monitor any changes in anxiety or moods was completed.

After baseline assessment, subjects were randomly assigned to one of four groups in a two-way factorial parallel design study of duration 16 weeks. Two groups were asked to maintain their normal dietary habits whereas subjects in the other two groups were given an individually tailored programme intended to reduce their total caloric intake by 4186–6279 kJ/day, providing protein, fat and carbohydrates as 15, 30 and 55% of energy, respectively. Within each of these two dietary study arms, subjects were further allocated to a control light exercise group or a vigorous intensity exercise group for three 30 min sessions per week. A control exercise group was used to minimize co-intervention bias, a factor not usually accounted for in exercise training studies. The light exercise protocol comprised a series of slow flexibility exercises once a week and stationary cycling (against zero resistance) (Monark Crescent AB, Varberg, Sweden) twice a week. Every second week subjects substituted one cycling session for a session during which they walked slowly, at a rate of approximately 2 km or less in 30 min. This range of exercises was offered to provide variety and to facilitate compliance for the 16-week period. The vigorous exercise programme was confined to a stationary cycling programme in which subjects cycled for 30 min at 60–70% of their maximum workload as determined from their fitness assessment. All programmes were supervised by a trained exercise supervisor and included 5 min warming up and 5 min cooling down periods before and after exercise.

Dietary compliance

The same dietitian monitored dietary intake throughout the study, subjects being given careful written and verbal instructions concerning how to keep detailed and accurate records of food weight and volume in a 3-day diet record every fortnight. Those subjects allocated to the caloric intake restriction group were given a target weight loss of approximately 7–8 kg during the 16 weeks. This was achieved by substituting low-fat alternatives for high-fat foods, increasing fruit and vegetable consumption, and substituting complex for refined carbohydrates. All of the subjects were advised to make no major changes to their sodium intake. Those subjects allocated to maintain their usual caloric intake were also examined fortnightly by the dietitian, who determined both from their 3-day diet records and by interview that no substantial alterations were being made. Maintenance of their usual dietary pattern was reinforced at each visit and they were offered a weight-loss programme on completion of the study.

Physical fitness assessment

Fitness was assessed by a multistage exercise test on an electrically braked cycle ergometer (Siemans-Elema AB, Medicinsk Teknik Solna, Sweden) commencing at zero workload and increasing at 20 W/min with a pedal rate of 60 rpm until the subject reached volitional fatigue. The maximum workload (W_{max}) was determined as the maximum achieved for a completed minute. Oxygen consumption was measured throughout and recorded each minute with maximum oxygen consumption ($\dot{V}O_{2max}$) taken as the maximum minute value with a respiratory gas exchange ratio of 1.12 or oxygen consumption having reached a plateau. Inspired volume was measured with a Morgan ventilation monitor (PK Morgan Ltd, Chatham, Kent, UK), expired oxygen by an Applied Electrochemistry S-3A oxygen analyser (Ametek Thermox Instrument Division, Pittsburgh, Pennsylvania, USA) and expired carbon dioxide by a Datex CD-101 carbon dioxide analyser (Datex Instrument DY, Helsinki, Finland). An on-line computer controlled the metabolic data. The heart rate was recorded during the last 15 s of each minute using a Cardiofax ECG-6511 (Nihon Konden Corp., Tokyo, Japan). Fitness was re-assessed at the end of the study between 48 and 72 h after the last exercise session.

Blood pressure was measured during the exercise test with the subject at rest sitting on the cycle ergometer and at 2 min intervals throughout the test. Measurements were performed by the same trained observer throughout the study, using a mercury-column sphygmomanometer. Blood pressures were compared at a predetermined submaximal workload of 140 W, which equated to approximately 50% of the mean maximum workload (W_{max}).

Clinic blood pressure

Clinic blood pressure was measured on three separate occasions during a 2-week baseline period. Measurements were performed every 2 min with subjects supine for 20 min and every minute with subjects standing for 5 min, again using the Dinamap 1846SX recorder to eliminate observer bias. Mean supine and standing blood pressures were calculated for each visit from these readings. Baseline blood pressure was defined as the mean blood pressure from these three occasions. During intervention, blood pressure was measured at fortnightly intervals for 14 weeks and weekly for the last 3 weeks. The blood pressure at the end of the study was defined as the mean of the final three measurements. All of the blood pressure measurements were taken with the subject in the non-fasting state, subjects having refrained from consumption of tobacco, tea, coffee, or cola drinks and vigorous exercise during the preceding 2 h, at least 48 h since the previous exercise session. Blood pressure measurements were always performed at the same time of day for each individual. The change in blood pressure was determined as the blood pressure at the end of the study subtracted from the baseline blood pressure. Resting heart rates were taken in conjunction with blood pressure recordings and the response to the intervention assessed in the same way.

Ambulatory blood pressure

Ambulatory blood pressure was monitored for 24 h at baseline and at the end of the intervention using the Accutracker II monitor (Suntech Medical Instruments, Raleigh, North Carolina, USA). The unit has an inbuilt programme to identify problem readings and artefacts and assigns appropriate test codes. The monitor was fitted at the same time of the day for each visit and at least 24 h after any vigorous exercise. Subjects were asked to continue their normal daily activities on the days on which they wore the monitor. The blood pressure cuff was worn on whichever arm the subject found more convenient but on the same arm for both assessments. The device was preprogrammed to take readings every 15 min for the first hour after the recorder had been attached and then set to record blood pressure at 20 min intervals during the awake hours and hourly during sleep

Any blood pressure measurement during the fitting of the monitor, any reading with a pulse pressure of less than 20 mmHg and any reading with a test code were discarded. Overall 81% of the readings were included, a mean of 52 readings being accepted and 12 rejected for each subject. Daytime blood pressure was considered as the 12 h from waking (0600–1800 h) and night-time as the remaining 12 h (1800–0600 h). The mean blood pressure was calculated for each hour.

Body mass

Body mass was measured at the same visits as blood pressure, using a calibrated beam balance (Seca Vogel Halke, Hamburg, Germany) with subjects in light clothing and without shoes. Baseline body mass was defined as the mean of three measurements taken over a 2-week baseline. The body mass at the end of the study was defined as the mean of three measurements performed during the last 3 weeks of the intervention.

Alcohol intake

Alcohol intake was monitored each fortnight by the completion of 7-day retrospective diaries, which were subsequently coded using standard industry tables of alcohol beverage content, with an estimate obtained before and after the intervention of alcohol consumption in ml/week ethanol. Mean corpuscular volume and the γ-glutamyltranspeptidase (γ-GT) level were also utilized as potential objective biomarkers of any change in alcohol intake.

Biochemical measurements

Blood for electrolytes levels, full blood picture and serum cortisol level determinations was extracted before and after intervention after an 8 h fast and at least 24 h after the last period of exercise. The samples for sodium and potassium levels determination were centrifuged immediately, and assayed the same day using the SMAC II Biochemical Analyser (Technicon, Tarrytown, New York, USA). A Coulter counter was used to determine the haematocrit level and mean corpuscular volume. The serum cortisol level was determined by the radioimmunoassay method (Direct Cortisol RIA Kit, Diagnostic Product Co., Los Angeles, California, USA). Twenty-four-hour urine samples were collected before and after the intervention and were assayed for sodium, potassium, calcium and creatinine excretion to monitor dietary changes. Urinary electrolytes and creatinine levels were assayed on a Technicon SMAC II multichannel auto-analyser using standard reagents (Technicon Inc., Sydney, Australia). Twenty-four-hour excretion of adrenaline and noradrenaline was also quantitated utilizing high-performance liquid chromatography with a reverse-phase column and electrochemical detection.

Statistical analysis

A two-way analysis of variance model (ANOVA) was used to compare changes in blood pressure, heart rate, body mass and fitness among the four groups. Because a fall in body mass was one of the end-points of the study, $\dot{V}O_{2max}$ (l/min) is reported, without correction for body weight. Clinic blood pressure, heart rate, body mass and alcohol consumption changes were analysed on the basis of on an intention to treat all of the subjects who entered the study ($n = 60$). Within-group comparisons were performed using Bonferroni's method with Student's t calculated as the mean-square error term from the two-way analysis of variance. One-way analysis of variance and χ^2-tests were used to test for differences in characteristics among groups at baseline.

Calculation indicated *a posteriori* that the study had 90% power at $\alpha = 0.05$ to detect a main effect of caloric intake restriction or vigorous exercise on clinic systolic blood pressure of 5 mmHg. The study had 80% power at $\alpha = 0.05$ to detect a main effect of either intervention on body weight of 3 kg. Values are expressed as the means (95% confidence intervals). Mean ambulatory blood pressures and heart rates were calculated for the whole 24 h period and separately for night-time and daytime. ANOVA was then used to determine the main effects and interactions associated with the two treatments. Treatment effects were also sought by examining treatment × time interactions in repeated measures analysis of variance.

Microfit [22] was used for TSA. Mean hourly differences from baseline for systolic and diastolic blood pressure and heart rate were calculated for each intervention group. The difference between treatment groups in this change from baseline was used as the dependent variable for modelling in Microfit using ordinary least-squares methods. All of the models included an intercept and a dummy variable (period), which took the value zero for daytime and unity for night-time, to indicate whether there were differences between the day and night effects of the interventions. Models were considered to be satisfactory only if there were no significant serial correlation (Lagrange multiplier tests for serial correlation), inadequacy of functional form (Ramsey's RESET test), or heteroscedasticity on examination of the regression of squared residuals on squared fitted values [25].

Results

Baseline characteristics

Fifty-one subjects completed the study. Eight subjects withdrew from the study because of a change in employment or work commitments and one because of an injury to his Achilles tendon sustained during normal daily activity. All of the subjects were Caucasian, with mean age 42.4 years (41.1–43.7) and weekly alcohol consumption 98 ml (73–125)l. Twelve subjects reported some vigorous intensity exercise (greater than 31.4 kJ/min) [26], but this was transitory in nature, comprising digging, gardening or building at home. Baseline $\dot{V}O_{2max}$ was 2.59 l/min (2.49–2.69) or 26.93 ml/kg per min (26.02–27.85) when corrected for weight, consistent with normal levels for sedentary subjects [27].

The mean clinic systolic blood pressure after screening was 137.7 mmHg (136.1–139.2), the mean diastolic blood pressure was 86.7 mmHg (85.4–89.4) and the mean heart rate was 75.6 beats/min (72.9–78.4). After a 4-week run-in period the baseline value of systolic blood pressure was 130.9 mmHg (128.6–133.1), that of diastolic blood pressure

Table 1 **Baseline characteristics in each study group.**

	Normal caloric intake		Low caloric intake	
	Light exercise (n=17)	Vigorous exercise (n=13)	Light exercise (n=14)	Vigorous exercise (n=16)
Age (years)	43.9 (41.6–46.2)	43.0 (40.5–45.6)	41.4 (37.9–44.0)	41.1 (38.2–44.0)
Height (cm)	175.7 (172.9–178.8)	174.3 (170.7–177.8)	177.7 (174.6–180.8)	175.5 (172.9–178.1)
Weight (kg)	91.9 (85.8–98.0)	92.6 (84.2–101.0)	97.7 (88.6–106.8)	102.8 (95.9–109.7)
Body mass index (kg/m^2)	29.7 (27.9–31.5)	30.5 (28.1–32.8)	30.9 (28.4–33.4)	33.3* (31.4–5.5)
Alcohol intake (ml/week)	89.9 (46.3–133.5)	95.8 (6.7–184.8)	109.5 (49.5–169.5)	99.1 (51.1–147.1)
Trait anxiety score*	53.5 (52.5–58.5)	58.9* (55.0–62.7)	52.8 (50.6–54.9)	55.3 (53.4–57.2)
$\dot{V}O_{2max}$ (l/min)	2.43 (2.23–2.64)	2.58 (2.39–2.76)	2.62 (2.39–2.85)	2.75 (2.52–2.97)
W_{max} (watts)	212.9 (200.4–225.5)	227.7 (211.7–243.7)	232.9 (218.1–247.6)	235.0 (220.7–249.3)
Clinic SBP (mmHg)	131.8 (127.4–136.1)	132.4 (126.4–138.4)	129.8 (127.4–136.1)	129.5 (124.1–135.0)
Clinic DBP (mmHg)	80.4 (77.4–83.4)	80.9 (77.4–84.5)	77.5 (74.9–80.0)	79.0 (76.1–82.0)
Clinic heart rate (beats/min)	70.0 (65.1–74.8)	69.3 (63.6–74.9)	72.9 (69.7–76.1)	73.7 (69.3–78.1)

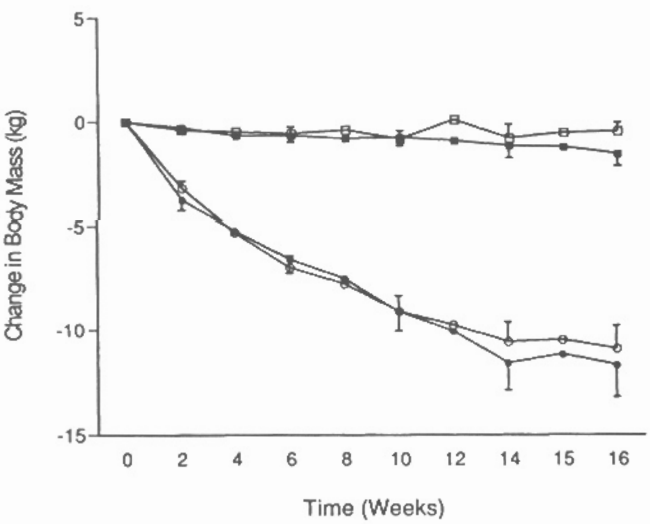
Values are expressed as means (95% confidence intervals. *$P < 0.05$ by one-way analysis of variance. DBP, diastolic blood pressure; SBP, systolic blood pressure; $\dot{V}O_{2max}$, rate of consumption of oxygen; W_{max}, maximum work.

was 79.4 mmHg (78.0–80.9) and that of heart rate was 71.5 beats/min (69.3–73.7). Baseline measurements for all four groups are shown in Table 1 and subjects remained well matched for all variables after random allocation to groups, except for BMI, which was significantly higher ($P < 0.05$) in the low caloric intake, vigorous exercise group, and anxiety, which was significantly higher ($P < 0.05$) in the normal caloric intake, vigorous exercise group.

Body mass

The time course of change in body mass is shown in Figure 1. A reduction of approximately 3 kg occurred after 2 weeks in the caloric intake-restricted groups, with a continuing fall until week 14 and stabilization during the final 2 weeks after a mean reduction of 11.3 kg (9.3–13.1). Weight was essentially unchanged in subjects maintaining their usual caloric intake. The vigorous intensity exercise did not independently reduce body mass during this period, whether undertaken alone or combined with caloric intake restriction.

Fig. 1.



Line graph shows change in body mass (mean ± SEM) in the four study group: □, normal caloric intake/light exercise (n=17); ■, normal caloric intake/vigorous exercise (n=13); ○, low caloric intake/light exercise (n=14); ●, low caloric intake/vigorous exercise (n=16).

Exercise training and fitness

The intensity of training for the vigorous exercise group was in the range 54–68% W_{max} with a mean workload of 60% W_{max}. Some of these overweight sedentary subjects could not tolerate work at 60% W_{max} at the start of the programme and were started at about 50% W_{max} and increased as their fitness improved. In terms of heart rate reserve (HR_{res}), the mean training intensity for the vigorous exercose group was 76% HR_{res} compared with 18% HR_{res} in the light-intensity exercise group. There was no evidence of any significant exercise not prescribed in the study during the intervention in any group.

There was a 24% improvement in oxygen consumption with vigorous intensity exercise of 0.56 l/min (0.47–0.65) ($F_{1,47} = 111.3$, $P < 0.001$), but no significant change in fitness for the light exercise groups. When the light exercise groups were analysed according to the separate modes of exercise, cycling was performed at a mean intensity of 17% HR_{res}, stretching at 19% and walking at 24%. There was a significant difference ($P < 0.05$) in intensity between walking and the other two modes. However, because the walk was only completed six times during the 16 weeks it was not likely to have influenced the level of fitness of the subjects. Their work capacity also improved by 24% with vigorous exercise but not with light exercise.

Changes in diet and alcohol intake

Analysis of the diet records revealed that caloric intake restriction reduced sodium intake from the food consumed by 1034.3 mg/day (497.1–1571.5) ($F_{1,48} = 9.79$, $P < 0.01$). However, discretionary salt use was not recorded and the results of analysis of changes in 24 h urinary sodium excretion did not differ among the study groups. Similarly, there were no differences in the changes in 24 h urinary

Table 2 **Urinary calcium, potassium, sodium, creatinine, adrenaline and noradrenaline levels before and after the intervention in the four study groups.**

	Normal caloric intake		Low caloric intake	
	Light exercise (n=12)	Vigorous exercise (n=12)	Light exercise (n=14)	Vigorous exercise (n=13)
Urinary adrenaline excretion (μmol/day)				
Before	0.05 (0.05–0.07)	0.06 (0.04–0.08)	0.06 (0.05–0.06)	0.06 (09.05–0.07)
After	0.04 (0.03–0.06)	0.06 (0.04–0.08)	0.06 (0.04–0.07)	0.04 (0.04–0.05)
Urinary noradrenaline (μmol/day)				
Before	0.30 (0.25–0.34)	0.33 (0.27–0.40)	0.35 (0.03–0.40)	0.37 (0.30–0.43)
After	0.29 (0.22–0.35)	0.33 (0.25–0.41)	0.30* (0.24–0.35)	0.30* (0.2– 0.35)
Urinary calcium excretion (mmol/day)				
Before	5.6 (4.0–7.3)	6.6 (5.3–8.0)	5.5 (4.0–6.9)	6.5 (4.4–8.7)
After	5.6 (3.6–7.7)	7.5 (6.1–9.0)	5.1 (3.2–7.0)	5.6 (4.1–7.1)
Urinary potassium excretion (mmol/day)				
Before	62.4 (51.9–72.8)	71.4 (63.2–79.6)	80.8 (67.2–94.4)	80.9 (69.0–92.7)
After	63.2 (52.0–74.5)	69.4 (58.0–80.7)	79.0 (62.4–95.6)	84.5 (64.2–84.9)
Urinary sodium excretion (mmol/day)				
Before	177.0 (133.8–220.2)	181.2 (142.8–219.6)	166.6 (136.7–196.4)	199.9 (159.9–239.9)
After	177.4 (130.6–224.3)	163.8 (117.6–210.0)	165.1 (128.1–202.1)	148.6* (114.8–182.4)
Urinary creatinine excretion (mmol/day)				
Before	16.9 (15.8–18.1)	17.0 (14.6–19.4)	18.5 (16.2–20.8)	18.2 (16.2–20.2)
After	15.9 (13.1–18.7)	15.9 (13.8–18.0)	15.5** (12.4–18.6)	17.1 (15.0–19.1)

Values are expressed as means (95% confidence intervals). *$P < 0.05$, **$P < 0.01$ by Student's t-test with Bonferroni's corrrection.

excretion of potassium, calcium and creatinine (Table 2). Analysis of diet records otherwise revealed no difference in the pattern of change in nutrient intake in the vigorous versus light exercise groups, irrespective of whether they were continuing their usual diet or restricting their caloric intake (data not shown).

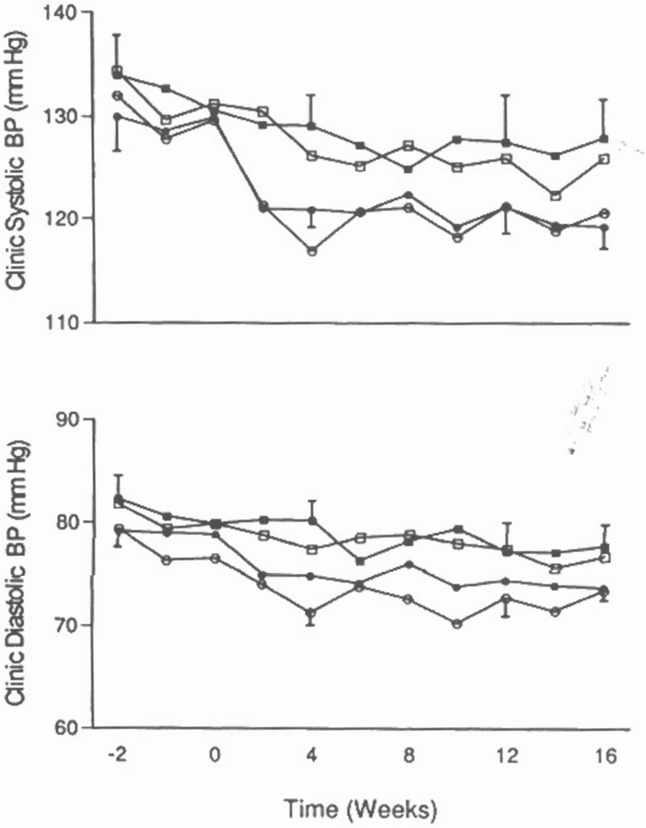
Weekly alcohol consumption fell in the caloric intake-restricted groups from 104 (68–140) to 80 ml/week (45–114) whereas in the normal caloric intake groups the intake increased slightly from 93 (50–135) to 111 ml/week (53–169). This represented a relative fall of 41 ml/week (5–78) ($F_{1,56} = 3.62$, $P < 0.06$). This reduction in alcohol intake is equivalent to half a standard drink a day and had no impact on the biomarkers of alcohol consumption, mean corpuscular volume or γ-GT.

Clinic blood pressure and heart rate

Significant falls in clinic systolic and diastolic blood pressure were found with caloric intake restriction but not with vigorous exercise. Falls were evident after 2 weeks of intervention, the maximal reduction being at 4 weeks and maintained for the rest of the intervention period (Fig. 2). The main effects of caloric intake restriction on supine clinic systolic and diastolic blood pressure were −5.6 (−2.3 to −8.9) ($F_{1,56} = 8.19$, $P < 0.01$) and −2.4 mmHg (−0.4 to −4.4) ($F_{1,56} = 4.09$, $P < 0.05$), respectively. Corresponding results for standing blood pressure were −8.0 (−3.6 to −12.4) ($F_{1,56} = 9.47$, $P < 0.01$) systolic and −3.2 mmHg (−0.7 to −5.7) ($F_{1,56} = 4.45$, $P < 0.05$) diastolic.

To assess whether the caloric intake-restriction effect on blood pressure was independent of the change in alcohol

Fig. 2.



Line graph shows clinic supine systolic and diastolic blood pressures (BP, means ± SEM) in the four study groups: □, normal caloric intake/light exercise (n=17); ■, normal caloric intake/vigorous exercise (n=13); ○, low caloric intake/light exercise (n=14); ●, low caloric intake/vigorous exercise (n=16).

consumption, the two-way analysis of variance was repeated with the change in alcohol consumption entered as a covariate. The effects of caloric intake restriction on supine systolic blood pressure but not on diastolic blood pressure were still significant ($F_{1,55} = 5.86$, $P < 0.05$; and $F_{1,55} = 2.31$, $P = 0.13$, respectively). The main effect for vigorous exercise was significant for standing heart rate [−4.2 (−0.6 to −7.7), $F_{1,56} = 3.83$, $P < 0.05$] but not for resting supine heart rate [−2.4 beats/min (2.5 to −7.2), $F_{1,56} = 1.95$, $P < 0.07$]. Caloric intake restriction decreased supine heart rate [−6.5 beats/min (−1.7 to −11.3), $F_{1,56} = 14.84$, $P < 0.001$] and standing heart rate [−5.4 (−1.0 to −8.9) beats/min, $F_{1,56} = 6.7$, $P < 0.05$]

Conventional analysis of ambulatory blood pressure

Of the 51 men who completed the study, 48 provided data from ABPM before and after the intervention. Baseline mean 24 h, daytime and night-time ambulatory systolic and diastolic blood pressure levels for each study group are presented in Table 3. Using ANOVA, 24 h and daytime systolic and diastolic blood pressure were significantly reduced by caloric intake restriction but not by vigorous exercise (Table 4). Night-time blood pressures were significantly influenced neither by caloric intake restriction nor by exercise alone. Caloric intake restriction and vigorous exercise each significantly reduced 24 h, daytime and night-time heart rates (Table 4). The combination of caloric intake restriction and vigorous exercise resulted in additive effects on ambulatory heart rate. With repeated measures analyses of ambulatory systolic and diastolic blood pressure, significant time × treatment interactions indicated an effect of caloric intake restriction for 24 h ($P = 0.05$) and daytime ($P = 0.04$) systolic blood pressure only, there being no significant association with vigorous exercise.

Time series analysis of ambulatory blood pressure

The hourly mean values for the change in systolic blood pressure from baseline values during the 24 h of ABPM for each study group are shown in Figures 3 and 4. The regression coefficients for the TSA using the difference between groups for the change from baseline in systolic blood pressure as the dependent variable are shown in Table 5.

Comparison of models examining the effect of reduced energy intake in the light-exercise groups showed that the fall in systolic blood pressure from baseline was signific-

Table 3 **Baseline 24 h, daytime, night-time ambulatory systolic and diastolic blood pressures in each group.**

	Normal caloric intake		Low caloric intake	
	Light exercise (n = 11)	Vigorous exercise (n = 11)	Light exercise (n = 13)	Vigorous exercise (n = 13)
Systolic blood pressure (mmHg)				
24 H	125.7 (121.7–29.7)	133.9 (130.2–137.6)	130.3 (126.2–134.4)	130.4 (125.3–135.5)
Day	130.7 (128.2–133.3)	138.3 (135.6–141.0)	136.8 (134.3–139.3)	137.4 (132.7–142.1)
Night	121.6 (115.1–128.0)	130.1 (124.1–136.1)	124.7 (118.7–130.7)	124.5 (117.0–131.9)
Diastolic blood pressure (mmHg)				
24 H	75.7 (72.4–79.0)	79.2 (76.0–82.4)	76.6 (73.6–79.6)	76.2 (72.4–80.0)
Day	80.6 (78.7–82.5)	83.8 (81.2–86.4)	81.2 (79.0–83.4)	82.6 (80.1–85.1)
Night	71.6 (66.6–76.5)	75.3 (70.5–80.1)	72.7 (68.6–76.9)	70.7 (65.2–76.2)

Values are expressed as means (95% confidence intervals).

Table 4 **Analysis of variance of summary data for ambulatory blood pressure changes. Mean changes in 24 h, daytime and night-time ambulatory systolic and diastolic blood pressures and heart rate in each study group are shown.**

	Normal caloric intake		Low caloric intake	
	Light exercise (n = 11)	Vigorous exercise (n = 11)	Light exercise (n = 13)	Vigorous exercise (n = 13)
Change in systolic blood pressure (mmHg)				
24 H	−3.2 (−5.6 to −0.7)	−3.6 (−5.6 to −1.6)	−9.5* (−11.3 to −7.8)	−7.4* (−9.2 to −5.6)
Day	−2.2 (−5.7 to 1.3)	−3.4 (−6.1 to −0.7)	−11.1* (−13.4 to −8.8)	−7.7* (−10.0 to −5.5)
Night	−4.5 (−7.9 to −1.1)	−3.9 (−7.0 to −0.8)	−7.4* (−10.0 to −4.7)	−11.0* (−15.2 to −6.7)
Change in diastolic blood pressure (mmHg)				
24 H	−3.1 (−4.9 to −1.3)	−2.9 (−4.2 to −1.6)	−6.7* (−8.0 to −5.3)	−5.7* (−6.9 to −4.4)
Day	−2.5 (−4.8 to −0.3)	−3.3 (−4.5 to −2.1)	−8.3* (−10.3 to −6.3)	−6.4* (−8.0 to −4.8)
Night	−3.6 (−6.3 to −2.2)	−2.6 (−4.9 to −0.34)	−5.3 (−6.9 to −3.7)	−5.1 (−7.0 to −3.1)
Change in heart rate (beats/min)				
24-H	3.0 (−16.2 to 22.2)	−4.0* (−5.4 to −2.7)	−2.7* (−4.5 to −1.0)	−9.4* (−11.1 to −7.7)
Day	1.6 (0.06 to 3.7)	−3.8* (−6.3 to −1.3)	−3.2* (−5.3 to −1.0)	−10.1* (−12.2 to −7.9)
Night	4.2 (2.7 to 7.2)	−4.2* (−5.6 to −2.9)	−2.4* (−5.2 to 0.4)	−8.8* (−11.6 to −6.1)

Values are expressed as means (95% confidence intervals). $^*P < 0.05$.

antly greater in the low caloric intake group ($P = 0.002$) and that this effect was greater during the daytime (period effect, $P = 0.009$, Table 5). For the vigorous-exercise groups, reduced caloric intake was also associated with a greater fall in blood pressure ($P = 0.008$), which was sustained throughout the 24 h period (period effect, $P > 0.05$, Table 5).

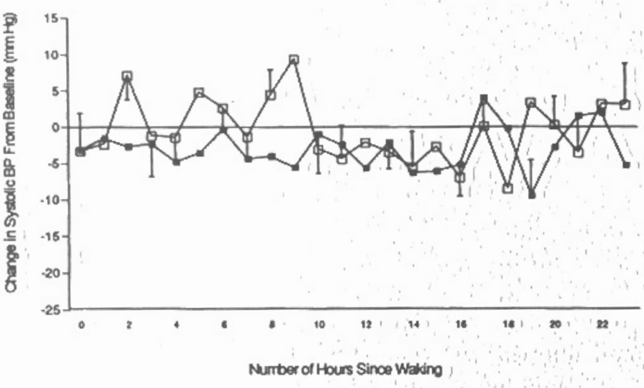
For models comparing effects of exercise intensity in subjects having normal caloric intake, there was a significantly greater fall associated with vigorous exercise ($P = 0.05$) for systolic blood pressure during the daytime (period effect, $P = 0.03$, Table 5). In the subjects with low caloric intake, there was a greater fall ($P = 0.024$) in the vigorous-exercise group, which was significantly greater during the night-time ($P = 0.003$). Using a similar comparison of models for DBP, there was no significant effect of caloric intake restriction or vigorous exercise.

Because there was an observed difference in BMI between the groups at baseline (Table 1), the time series modelling reported above was repeated with adjustment for body weight. Weight-adjusted blood pressures were no different from non-weight-adjusted values.

Exercise blood pressure and heart rate responses

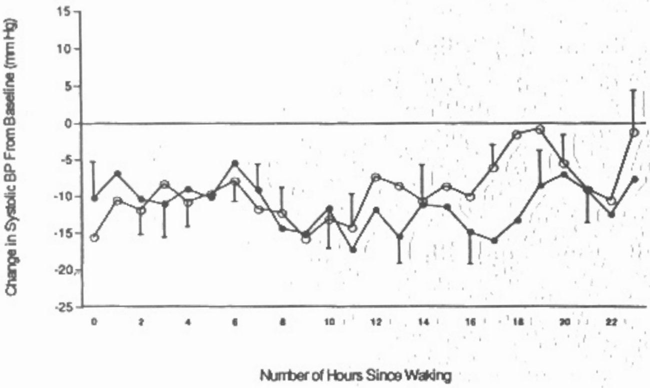
The blood pressure response to exercise at a submaximal workload of 140 W was reduced both by caloric intake restriction and by vigorous exercise, with the combined approaches resulting in additive effects (Fig. 5). The reduction in exercise systolic blood pressure was 8.9 mmHg (1.5–16.5), ($F_{1,47} = 3.8$, $P < 0.05$) for caloric intake restriction and 13.2 mmHg (5.6–20.8) ($F_{1,47} = 8.4$, $P < 0.01$) for vigorous exercise. Only vigorous exercise significantly reduced the diastolic blood pressure response [by 8.6 mmHg (4.9–12.3), $F_{1,47} = 15.28$, $P < 0.001$]. The

Fig. 3.



Line graph shows change in ambulatory systolic blood pressure (BP, mean ± SEM) in the two normal caloric intake groups: □, light exercise (n = 11); ■, vigorous exercise (n = 11).

Fig. 4.



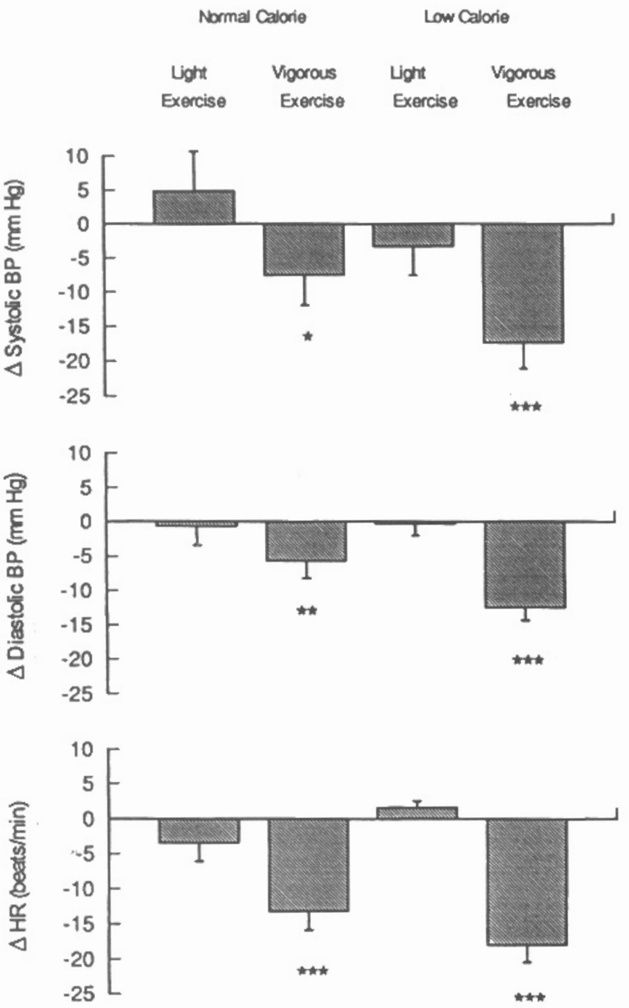
Line graph shows change in ambulatory systolic blood pressure (BP, mean ± SEM) in the two caloric intake-restricted groups: ○, light exercise (n = 13); ●, vigorous exercise (n = 13).

Table 5 **Ordinary least-squares regression models with change in ambulatory systolic blood pressure (SBP) as the dependent variable.**

	Student's t-test					F-test	
Independent variable	b	Standard error	t	P	R²	F	P
Normal caloric intake, light versus vigorous exercise							
Change in heart rate	−0.69	0.26	2.697	0.014	0.6558	$F_{3,19} = 5.725$	0.006
First-order lag in SBP	0.25	0.21	1.190	0.249			
Period	5.25	2.16	2.429	0.030			
Intercept	−4.46	2.12	2.098	0.050			
Low caloric intake, light versus vigorous exercise							
Change in DBP	0.74	0.14	5.321	0.000	0.6128	$F_{2,21} = 16.57$	0.000
Period	−4.78	1.40	3.398	0.003			
Intercept	2.39	0.98	2.437	0.024			
Light exercise, normal versus low caloric intake							
Change in DBP	−0.54	0.31	1.773	0.092	0.4465	$F_{3,19} = 5.110$	0.009
First-order lag in SBP	0.30	0.22	1.377	0.185			
Period	7.89	2.71	2.913	0.009			
Intercept	−9.56	2.60	3.670	0.002			
Vigorous exercise, normal versus low caloric intake							
Change in DBP	0.40	0.18	2.262	0.035	0.5765	$F_{3,20} = 9.074$	0.001
First-order lag in SBP	0.62	0.17	3.683	0.001			
Period	2.52	1.63	1.544	0.138			
Intercept	−4.39	1.50	2.933	0.008			

DBP, diastolic blood pressure.

Fig. 5.



Bar chart shows mean ± SEM changes (Δ) in the response of systolic and diastolic blood pressures (BP) and heart rate (HR) to a workload of 140 W on a bicycle ergometer during week 16 of the intervention. $^{*}P < 0.05$, $^{**}P < 0.001$, $^{***}P < 0..001$ by Student's t-test with Bonferroni's correction.

heart rate response to a workload of 140 W was significantly reduced by vigorous exercise [by 14.6 beats/min (10.9–18.3), $F_{1,47} = 43.42$, $P < 0.001$] but not by caloric restriction.

Biochemical and haematological measures

Caloric intake restriction had no effect on urinary adrenaline excretion. However, there was a significant change in urinary noradrenaline excretion with caloric intake restriction in the 47 subjects with complete urine collections, with levels falling from 0.36 (0.32–0.40) to 0.30 μmol/day (0.27–0.33) in caloric intake-restricted subjects and remaining unchanged in those eating their usual diet [0.32 (0.28–0.35) to 0.31 μmol/day (0.26–0.35), $F_{1,43} = 4.28$, $P < 0.05$]. Vigorous exercise had no independent or additive effect on 24 h urinary catecholamine excretion. The plasma cortisol level, erythrocyte mean corpuscular volume, haemoglobin level and haematocrit level were unchanged either by caloric intake restriction or by exercise.

Psychological variables

There was a significant ($P < 0.05$) difference between groups at baseline in the Trait score of anxiety (Table 1). The State anxiety score was similar for all four groups at baseline. There was no significant main effect on anxiety of caloric intake restriction or vigorous exercise during the intervention. Baseline scores on the six POMS subscales were similar in all four groups and there were no significant differences after the intervention.

Discussion

This study examined the independent and combined effects both on clinic and on ambulatory blood pressure of exercise and weight loss by caloric intake restriction in sedentary overweight men. The effects of caloric intake restriction in reducing blood pressure were consistent for clinic and ambulatory measures, there being a predominant influence on the daytime ambulatory blood pressure. These effects were of a similar magnitude and time course of onset to those previously reported by our group [5] and others [28]. In contrast, there was no measurable influence of vigorous exercise on clinic blood pressure or on ambulatory blood pressure analysed by conventional approaches. However, a more sensitive approach with TSA confirmed a decrease in daytime ambulatory blood pressure either with vigorous exercise or with caloric intake restriction. Furthermore, although the two approaches were not additive with respect to their effect on daytime blood pressure, they exhibited a synergistic effect when combined to lower night-time blood pressure also, resulting in blood pressure reduction throughout the 24 h period for those subjects assigned to caloric intake restriction with an exercise programme. This synergistic effect had not previously been demonstrated.

In a previous study [5] in overweight male drinkers, in which we achieved an overall reduction in body mass of 9.6 kg during an 18-week intervention, there was a corresponding 5 mmHg fall in systolic blood pressure and a 4 mmHg fall in diastolic blood pressure attributable to caloric intake restriction. Falls in the present study were of similar magnitude, a 9.5 kg loss in body mass resulting in a 6 mmHg fall in supine clinic systolic blood pressure and a 2 mmHg reduction in diastolic blood pressure. In our previous study the falls in blood pressure with caloric intake restriction were additive to the effects of a reduction in alcohol intake, which independently resulted in falls in blood pressure of similar magnitude. In order to minimize the potential for confounding by any change in alcohol intake, subjects in the present study were therefore carefully recruited on the basis of a self-reported alcohol intake below the lower limit necessary for inclusion in our previous study (i.e. < 210 ml/week). Their mean alcohol intake at baseline was approximately 100 ml/week and it fell by approximately 40 ml/week during the intervention in caloric intake-restricted subjects, a fall that was of borderline significance only. With alcohol reduction entered as a covariate, the effect of caloric intake restriction on diastolic blood pressure was attenuated. However, such a reduction might not have been clinically relevant, considering estimates from intervention studies that a 100 ml/week reduction in alcohol intake is required for a fall in systolic blood pressure of 1.1 mmHg [29] and a threshold level of alcohol consumption of 20–30 ml/day reported in cross-sectional population studies before a pressor effect of alcohol is apparent [30]. The potential confounding effect of a decrease in alcohol intake has usually been ignored in previous lifestyle intervention studies addressing the effects of caloric intake restriction or exercise on blood pressure. It could be one explanation of the inconsistent outcomes reported concerning the effects of exercise, subjects participating in lifestyle interventions often altering more than just the lifestyle modality of interest.

It has been suggested that the antihypertensive effect of caloric intake restriction could be caused, at least partly, by a reduction in salt intake [31]. However, Reisin *et al.* [32] were able to demonstrate a reduction in blood pressure with caloric intake restriction that was independent of salt intake.. In the present study there was a significant reduction in salt obtained from food after caloric intake restriction, but we did not record changes in discretionary salt use. Because 24 h urinary sodium excretion did not change, we assume that discretionary salt use increased. The magnitude of the fall in dietary salt intake (approximately 18 mmol/day) is not likely to have been an important confounder of the blood pressure reduction in the present study (a 3.1 mmHg fall was predicted by the Intersalt study for a 100 mmol/day fall in sodium intake [33]).

In a previous study [15], using an identical vigorous exercise protocol and control light exercise programme, we also failed to observe an effect of exercise reducing clinic blood pressure during a 4-week intervention. Even though the present study extended the vigorous exercise protocol to 16 weeks, no influence on clinic blood pressure was evident, a finding similar to those observed by several other groups [13,14,34]. The fall in blood pressure in the control light-exercise group could have been a familiarization effect [4] or caused by the effect of an active control. However, neither of these reasons are likely because we had a similar 4-week run-in period in a previous study [15] with no fall in blood pressure observed in the control light-exercise group. Another group also used an active control group and found no falls in blood pressure [9]. However, other studies with non-active controls have also reported falls in blood pressure [14,16]. These results contrast with the findings of others in well-controlled studies in which consistent falls in blood pressure with exercise for less than a 16-week period were reported [8–10,20]. These falls required no improvement in cardiovascular fitness and were apparent after only four exercise sessions [11,35]. These contrasting results raise questions concerning the influence of the initial level of blood pressure, the duration of each exercise session, the intensity of the exercise, the mode of exercise and the design of the training programme in dictating these different outcomes.

Recent studies [12,36] indicated that exercise intensity might be an important determinant of the response of blood pressure to exercise training and that exercise of low or moderate intensity might be as efficacious as, or even superior to, high-intensity exercise in reducing resting blood pressure. In a meta-analysis of several of the earlier studies, Hagberg [37] paradoxically observed that the fall in blood pressure tended to be related inversely to the intensity of the exercise and suggested that the optimal benefits for blood pressure are found at intensities of 40–60% $\dot{V}O_{2max}$ [36–39]. Given that the intensities of exercise used in our previous study and the current study were 80 and 76% $\dot{V}O_{2max}$, respectively, this could account for the lack of a reduction in resting blood pressure. Other studies using higher intensity exercise have also failed to show blood pressure reductions with training [13,14,17,34]. However, in yet other reports, a similar reduction in blood pressure was evident both for lower and for higher intensity exercise programmes [18,39].

Previous comparisons of the relative effects of exercise on ambulatory versus clinic blood pressure have reported inconsistent results. Changes in ambulatory blood pressure were less than those in clinic blood pressure in two studies [4,16]. Others showed similar changes in resting and ambulatory blood pressure [20] whereas Marceau *et al.* [19] reported an outcome similar to that of the present study, with falls in ambulatory blood pressure, but no identifiable change in clinic blood pressure after 10 weeks of exercise at either 50 or 70% of $\dot{V}O_{2max}$. The falls in ambulatory blood pressure were only apparent when we utilized time series methods, an approach that showed both caloric intake restriction and vigorous exercise to be independently associated with lower daytime systolic blood pressure. Furthermore, when vigorous exercise was combined with caloric intake restriction, the reduction in systolic blood pressure was sustained into the night-time, suggesting a synergistic effect of the combined interventions. Time series analysis seems to be a more sensitive method for recognizing such differences and has advantages over conventional ANOVA, which uses ambulatory recordings summarized over arbitrary intervals. The observation of a reduction in daytime systolic blood pressure with exercise is in agreement with the findings of others [4,16]. Although Fortmann *et al.* [4] were also able to demonstrate falls in night-time systolic and diastolic blood pressure with exercise and in night-time systolic blood pressure with caloric intake restriction, in their study the exercise programme was designed to induce weight reduction simultaneously, with no assessment of the effects on blood pressure of exercise alone. Van Hoof *et al.* [20] reported a reduction in daytime diastolic blood pressure with exercise in hypertensives but a decrease in body weight could have been an important determinant of this outcome. A more recent study concerning the effects of exercise on ambulatory blood pressure [19] highlighted the further confounding effect of exercise intensity when attempting to understand the influence of exercise on ambulatory blood pressure. They compared a high- versus low-intensity exercise regimen and, although the two approaches had a similar effect in reducing the 24 h mean, the high-intensity exercise predominantly influenced the evening and sleep blood pressure whereas the low-intensity exercise reduced daytime blood pressure.

The response of blood pressure to exercise has received some attention in recent years with respect to the potential to predict or diagnose the onset of hypertension [40,41] or in relation to its association with left ventricular hypertrophy [38,42]. However little attention has been devoted to the effect of exercise training on this response. In the present study, vigorous exercise attenuated the systolic blood pressure, diastolic blood pressure and heart rate responses to a predetermined workload (140 W). When the vigorous exercise training was combined with caloric intake restriction, there were additive effects reducing the response of systolic blood pressure to acute submaximal exercise. The magnitude of the fall in exercise systolic blood pressure was similar to that reported for normotensives by others [20]. The benefits of lower blood pressure during exercise may be more significant and clinically relevant than previously thought, with the systolic blood pressure response to maximal and submaximal exercise also reported to be more closely related to left ventricular mass than is resting blood pressure [43,44]. Similarly, the finding of a reduction in ambulatory, but not in clinic, blood pressure should not make us discount the potential value of exercise in the prevention of hypertension and cardiovascular disease, given the evidence that ambulatory blood pressure during a normal working day is more closely related to left ventricular mass [45]. Thus clinic, exercise and ambulatory blood pressure may provide quite different information concerning the effects of exercise training on blood pressure [16] and therefore should all be used when evaluating the efficacy of exercise in preventing or treating hypertension.

In the present study urinary catecholamines levels were monitored as a crude indicator of sympathetic activity. Levels neither of urinary adrenaline nor of noradrenaline were changed by vigorous exercise, although that of noradrenaline fell with caloric intake restriction. A fall in the levels of catecholamine metabolites and plasma noradrenaline has been proposed to explain the reduction in blood pressure with caloric intake restriction because falls in urinary catecholamine metabolites levels and blood pressure are observed within 48 h of caloric intake restriction [48]. Exercise training-induced blood pressure falls have also been attributed to reduced sympathetic nerve activity, on the basis of falls in plasma noradrenaline level [8] and noradrenaline spillover [49]. Our data are consistent with a fall in sympathetic activity mediating the effect of caloric intake restriction or weight loss on blood pressure, but not with any independent or additive effect of exercise on this mechanism. However, the degree of physical activity during the period of 24 h urine collection could have masked any falls in resting sympathetic activity.

The effects of exercise reducing anxiety and altering mood have been proposed as one possible mechanistic pathway of blood pressure reduction with exercise. In this study, 16 weeks of vigorous exercise had no significant effect on the anxiety score or on the POMS score. Acute vigorous exercise has previously been reported to reduce both anxiety and blood pressure in normotensives for 2–3 h after exercise [50]. Studies using POMS have shown enhanced mood states and reduced anxiety with regular exercise [51,52]. Blumenthal *et al.* [51] also demonstrated reductions in anxiety after 10 weeks of exercise. However, changes in psychological aspects such as anxiety may not be great with chronic exercise if the individual is already within the normal range [53]. In our study, baseline anxiety scores were within the lower normal range and hence it might not be realistic to expect any further lowering of anxiety.

In conclusion, in this study concerning sedentary overweight men with two appropriate lifestyle interventions for 16 weeks, caloric intake restriction resulted in falls both in clinic and in ambulatory blood pressure. An increase in fitness after vigorous exercise did not augment this fall in clinic blood pressure, but, when combined with caloric intake restriction, it reduced ambulatory blood pressure throughout a 24 h period. The combined interventions also exhibited additive effects attenuating the response of blood pressure to acute submaximal exercise. Overall, the combination of weight control and exercise training should reduce cardiovascular risk substantially, including the risk of the development of established hypertension in overweight sedentary subjects with high normal blood pressure.

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