Original Article

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Are three months multidisciplinary lifestyle intervention enough to get benefits on blood pressure in overweight/obese adults ?

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Abstract

The aim of the study is to determine the effects of a multidisciplinary lifestyle intervention (including a short period of physical exercise) on some health-related variables, particularly on blood pressure, in an overweight/obese adult group. The main outcome was blood pressure lowering. The study involved 378 subjects affected by obesity or type 2 diabetes. The intervention included exercise, nutrition and psychological aspects. Before and after the intervention, several anthropometrics, cardiovascular risk related measures (height, body weight, body mass index, waist circumference, body composition and WHTR index) and physical exercise measures (aerobic capacity, flexibility and dynamic muscle strength) were evaluated through fitness tests. We observed a significant reduction in: blood pressure values, body weight, BMI, waist circumference, WHTR, fat mass and an improvement of fat free mass and physical exercise measures. The C.U.R.I.A.Mo. multidisciplinary approach is effective for reducing blood pressure, after relatively few exercise sessions (three weeks), particularly in patients with hypertension. The intervention can ameliorate the health status and physical performance in the short term, in normotensive and hypertensive adult subjects with overweight/obesity.

Keywords: Exercise; Lifestyle; Obesity; Blood Pressure; Chronic disease.

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INTRODUCTION

Physical activity is considered as one of the most important instruments for primary prevention of hypertension [1]. Since 2003 The National High Blood Pressure Education Program Coordinating Committee [2] and International Society of Hypertension [3] have recommended an approach aimed at improving lifestyle habits (engage in moderate physical activity; maintain normal body weight; limit alcohol consumption; reduce sodium intake; maintain adequate intake of potassium; and consume a diet rich in fruits, vegetables, and low-fat dairy products and reduced in saturated and total fat) and decreasing elevated blood pressure (BP) levels for those with high normal BP or hypertension.

The WHO (World Health Organization) has reported that attributable mortality worldwide is greater for hypertension than for many traditional cardiovascular disease (Cardio Vascular Diseases, or CVD) risk factors (e.g., tobacco, abnormal lipids, undesirable body mass index (BMI) [4]. Normally physical exercise can cause an acute increase in both metabolic activity and systolic BP (SBP), while the diastolic BP (DBP) values lower slightly or are unchanged [5]. Some authors have underlined that an insufficient increase or drop in BP noted during incremental exercise testing could be associated with underlying cardiac and CVD [5]. On the other hand, it has been shown that a BP reduction of 5 mmHg is linked with stroke and heart disease reduction of 15%-20% [6]. The positive BP effects of physical exercise, including significant reductions in clinic systolic SBP, DBP and daytime ambulatory systolic (or DAYSBP) and diastolic (or DAYBP) BP have already been documented [7]. Further, Taylor [8] has suggested that in older sedentary men with stage 1 or 2 hypertension, the reduction in BP load from an acute exercise bout of just 45 minutes is immediately apparent and can persist for 24 hours. This phenomenon occurs through adjustments in the neuro-humoral mechanisms and could have an important clinical impact on cardiovascular health.

Prehypertension, well defined as SBP between 120 and 139 mmHg and/or DBP between 80 and 89 mmHg, requires health-promoting lifestyle modifications to prevent the progressive rise in BP values and cardiovascular disease.

Moreover, lifestyle modifications are essential for overweight/obesity and high BP prevention: these are generally the initial steps in diseases management. Multidisciplinary management of chronic metabolic diseases (e.g. diabetes, overweight and obesity) [9] are the recommended methodology: multidisciplinary interventions and exercise have been demonstrated to be effective in adults [10] and children [12] on ameliorate microcirculatory function, glycometabolic control, systemic blood pressure and exercise measures. Martinez Aguirre-Betolaza et al. [13] have stated that supervised exercise and a healthy diet may produce a significant improvement in the autonomic nervous system functioning, reducing heart rate and blood pressure.

Once cardiovascular risk factors are evaluated in patients with hypertension, it is essential to pay attention to lifestyles and behavioral habits that favorably affect BP levels and reduce the overall risk of cardiovascular disease [1]. Cardoso et al. [14] have observed that BP values are lower when evaluated after exercise with respect to BP measured before exercise sessions or on day without exercise. In order to be clinically relevant, BP reduction after exercise must have a considerable effect and it should be maintained for a long period of time under ambulatory conditions [14].

Some authors have already well clarified the Post-Exercise Hypotension (PEH) phenomenon as an acute physical exercise effect characterized by a sustained decrease in BP after a single bouts of exercise; the duration of PEH occurs from 10 minutes and persists until 24h after a bout of exercise [15]. An acute exercise session can promote the lowering of clinical BP during the post-exercise period in both hypertensive and normotensive subjects [16].

Although the effect of a single period of aerobic exercise on post-exercise DAYBP has been widely studied [17,18] discordant opinions remain when these effects are studied in different groups, for example normotensive or hypertensive subjects. Some authors have found support for the physical exercise effects on BP values detected in normotensive subjects after training [17], while others have not observed any change in post-exercise BP values of such subjects [19]. On the other hand, some studies which involved hypertensive subjects have demonstrated significant post-exercise ambulatory BP decreases [8,18-20].

To our knowledge, among the aspects not yet fully clarified were the exact time span within which benefits can be observed on pressure values induced by physical exercise and the different, specific, characteristics of the exercise (such as type, intensity, training length and muscle groups involved) that might also be important in determining post-exercise hypotension.

After aerobic exercise some authors have observed neural mechanism as a reduced sympathetic nerve muscle activity, cardiac autonomic balance and increased baroreflex sensitivity, as well as heart rate variability. Conversely, other studies that used exercise strength or maximum aerobic exercise have observed an increase in cardiac sympathy and vasomotor modulation, decreased parasympathetic modulation, and/or attenuation of baroreflex sensitivity [21]. Other evidence has shown an important mechanism working in the nervous system to adjust post exercise hypotension [22]. Though these effects require further studies to be fully understood, it seems to be widespread agreement among some authors that a single aerobic exercise episode decreases arterial pressure during the post-exercise period, especially in hypertensive subjects. Furthermore, this effect lasts for several hours and therefore it has clinical significance for hypertensive patients. Regarding PA type and intensity. Quinn et al. [18] observed greater hypotensive effects after heavy exercise compared to light exercise. In contrast with this observation, other authors have found that low-intensity exercise results in greater post-exercise hypotension: Park et al. [20] reported that post-exercise ambulatory hypotension lasted longer when the same exercise was divided into multiple short periods than when exercise was continuous.

Some authors argue that endurance training, compared to other types of training, reduces BP values more in hypertensive participants (8.3/5.2 mmHg) and that the regular practice of lower intensity (and duration) physical activity, although it reduces BP less than moderate or high-intensity exercise, is associated with at least a 15% decrease in mortality [23]. This evidence suggests that people with high BP should be advised to participate in at least 30 minutes of dynamic aerobic exercise (as walking, cycling, etc.) at moderate intensity, on 5–7 days weekly. Performance of resistance exercises on 2 - 3 days per week can also be advised. For additional benefit in healthy adults, a gradual increase in aerobic physical activity to 300 minutes a week of moderate intensity or 150 minutes a week of vigorous intensity aerobic physical activity, or an equivalent combination thereof, is recommended [16].

The American College of Sports Medicine guidelines proposes exercise programs for the person with hypertension that provides ≥ 30 min of accumulated physical activity on most days of the week at 40 to 60 % of maximum capacity [16]. Because a single bout of exercise can cause an acute reduction in BP that lasts many hours (e.g., Post Exercise Hypotension or PEH) thus augmenting or contributing to the reductions in BP resulting from exercise training [24], consideration should be given to daily or near-daily exercise. Some authors have explained that the acute and chronic depressor effects of dynamic exercise are a low-threshold phenomenon: the hypotensive responses are noted at an exercise intensity of 40% of maximum oxygen consumption [25]. Additionally, it seems that it's possible to have this hypotensive effects related to physical exercise after only a few sessions of aerobic activity [26].

In overweight/obese adults the optimal exercise-training characteristics for reducing blood pressure (BP) are unclear to date. Some authors have stated that high-intensity interval training [27] and aerobic exercise programs [13] are to be considered as a treatment option for BP management.

To our knowledge, the exact magnitude of reduction in BP following exercise training is unclear to date. In this study we try to give very detailed data in a methodical assessment of blood pressure before and after exercise sessions.

Speculating that a multidisciplinary lifestyle intervention ameliorates some health-related variables, particularly blood pressure values, we try to explain if a few weeks of exercise is enough to achieve benefits on blood pressure in an overweight / obese adult group. This short term, retrospective study aims to show the effects of a multidisciplinary lifestyle intervention on some health-related measures. Particularly, it tries to contribute to the understanding of the exercise time-related effects on BP.

MATERIALS AND METHODS

Participants

The study involved 378 subjects (women n=226, man n=152, age median=52, min=18, max=75) affected by overweight/obesity (n=253, BMI median=33.9, min=24, max=52.3) or type 2 diabetes (n=125, BMI median=31.1, min=20.6, max=44.3) enrolled among the patients whom participated in C.U.R.I.A.Mo. (Centro Universitario Ricerca Interdipartimentale Attività Motoria) trial between January 2011 and December 2014. Inclusion criteria were: age between 18 and 75 years, BMI >27 kg/m^2. Exclusion criteria are: concomitant diseases contraindicating physical exercise and failure to sign written informed consent. The C.U.R.I.A.Mo. trial was registered in the Australian New Zealand Clinical Trials Registry, ACTRN12611000255987 and it approved by the local Ethics Committee (CEAS Umbria Region, HREC number 1/10/1633).

Basing on DAYBP values, according to pharmacological treatment and *ESH/ESC* classification of BP levels (table 1) [28] the 378 participants - whose baseline sociodemographic data are reported in table 2 - will be allocated into resultant subgroups (table 3):

1) *normotensive subjects group* presenting SBP value < 120 mmHg and DBP value < 80 mmHg (n=89, mean SBP = 120 mmHg, min 100 - max 135; mean DBP 75 mmHg, min 55 - max 80*)* and no taking medications*;* 2) *hypertensive subjects group*, presenting SBP >140 mmHg and/or DBP >90 mmHg, or being on antihypertensive treatment (n=289, mean SBP 140 mmHg, min 100 - max 170; mean DBP 85 mmHg, min 60 - max 110*);* this group involved also the subjects presenting SBP > 140 and/or DBP> 90 and which are not in antihypertensive medicinal product regimen. To avoid the drug masking-effect, patients with normal high blood pressure who followed a pharmacological therapy with anti-hypertensive drugs were included in the group of hypertensive patients.

According to Center for Chronic Disease Prevention and Health Promotion BMI classification [29] participants' sociodemographic data were presented into BMI subgroups (table 3), as follow: normal weight, BMI 18.5 – 24.9 (Norm); overweight, BMI<29.9 (Over); obese, BMI ≥30 (Ob) groups.

All subjects underwent to the C.U.R.I.A.Mo. lifestyle intervention program, lasting three month, that included [30]: 1) a first medical examination with the endocrinologist, to clinically evaluate the disease and any complications; 2) an interview with a psychologist to increase the subject's motivation; 3) a nutritional interview to assess the nutritional behavior of the participants and to improve the Mediterranean diet adherence; 4) an individualized program consisting of 25 sessions (two per week) of structured indoor exercise, preceded by the medical specialist in sport medicine evaluation, to asses physical exercise measures.

Structured, mixed, indoor exercise program was supervised by a graduate in Sport Science with a maximum attendance of 5 patient/group, twice a week for three months. Each of 25 sessions lasts 90 minutes (60 minutes of aerobic workout and 30 minutes of circuit training for muscular strength and flexibility exercises). The aerobic workout was performed using ergometers (treadmill, ciclo- and arm ergometer) with work intensity gradually increased from 50% up to 70% of heart rate reserve. The workout for muscular strength will use isotonic machines for training of the lower and upper limbs, with gradual increase from 50 % of 1 repetition maximum (RM) estimated before starting the program. Two sets of 20 repetitions have been carried out for each exercise, with 45 seconds of rest between sets and exercises. Machine loads was gradually increased (every three weeks if it's possible), according to the individual performance and capacity.

Table 1. Definitions and classification of office blood pressure levels (mmHg). Adapted from 2018 ESH/ESC Guidelines for the management of arterial hypertension [28].

Blood Pressure Category	Systolic BP	Conjunction	Diastolic BP
Optimal	<120	*and*	<80
Normal	120–129	*and/or*	80–84
High normal	130–139	*and/or*	85–89
Grade 1 hypertension	140–159	*and/or*	90–99
Grade 2 hypertension	160–179	*and/or*	100-109
Grade 3 hypertension	≥180	*and/or*	≥110
Isolated systolic hypertension	≥140	*and*	<90

Table 2. Participants sociodemographic data.

Indicator	Women			Man		
	All=226	Normo=70	Hyper=156	All=152	Normo=19	Hyper=133
Age	49.34 ± 12.63	39.47±11.52	53.76±10.43	52.88±11.08	45.21±16.48	53.97±9.69
Body weight (kg)	89.7 ± 15.06	90.39±14.03	89.39±15.54	103.84±18.32	101.9±17.07	104.12±18.54
BMI (Kg/m2)	33.70 ± 4.95	34.04±4.60	33.54±5.10	33.52±5.15	32.18±4.25	33.71±5.25
WC (cm)	108.18± 11.51	107.06±11.96	108.69±11.31	115.03±12.56	112.05±10.86	115.46±12.76
WHTR (cm)	0.664±0.07	0.659±0.07	0.667±0.07	0.654±0.07	0.657±0.070	0.657±.0.7
DAYSBP (mmHg)	131.26± 12,62	121±8.49	135.57±11.55	136.65±14.11	121.05±7.56	121.05±7.56
DAYDBP (mmHg)	79.88± 8.75	73.15±6.59	82.7±7.97	83.78±9.85	73.16±7.49	85.3±9.2

Data are expressed as mean ± standard deviation values. Normo= Normotensive group; Hyper=Hypertensive group; BMI=Body Mass Index; WC=waist circumference; WHTR=waist-height ratio value; DAYSBP=daytime ambulatory systolic blood pressure value; DAYDBP=daytime ambulatory diastolic blood pressure value.

Measures

During C.U.R.I.A.Mo. lifestyle intervention anthropometric measures such as height (expressed in cm), body weight (expressed in Kg), Body Mass Index (or BMI, expressed in Kg/m^2), waist circumference (or WC, expressed in cm), body composition (as fat and muscle mass, expressed in %) and the waist-to-height ratio index (or WHTR) were evaluated. BP values as DAYSBP, DAYDBP, SBP and DBP (expressed in mmHg) were measured. Furthermore, physical exercise measures as maximum dynamic muscle strength (expressed in Kg), aerobic capacity or VO_2max (expressed in in $ml/O_2/Kg/min$) and flexibility (expressed in cm) were measured. All the variables were measured at the beginning and after three-months of intervention, as described below.

- *Anthropometric measures,* such as body weight and body composition, were performed during first medical examination, using Bioelectric Impendence Technology (BIA) trough body composition analyzer (BC-420MA TANITA, Tokyo, Japan). BMI was calculated as weight over height squared. WHTR, an anthropometric index for measuring central adiposity used to identify cardio metabolic risk as well as WC and BMI, was calculated dividing WC by height [31].
- *BP values* were measured through a mercury-free sphygmomanometer (UM-101, A&D Medical, Italy), using a properly sized BP cuff. During first medical examination ambulatory BP values (DAYBP) were measured for three times, one minute lasting between consecutive measurement and after 5 minutes of sitting at rest, on the right upper arm using an appropriate sized cuff. Furthermore, BP values were evaluated during three months exercise intervention program, at the beginning (or T0 value), every three weeks (T1, T2, T3) in correspondence of the exercise intensity increase and at the end (T4 values). To evaluate the exercise effects BP, these values were evaluated before (PRE) and after (POST) exercise sessions. We used an upper arm BP monitor (AND A&D Medical, Model UA-787Plus).
- *Physical exercise measures,* as the maximum dynamic muscle strength and VO_2max, was estimated before starting the training program (during the medical specialist in sport medicine evaluation) and after three-months, as follows. During the first week (sessions n°1 and n°2) all the patients participated at pre-training sessions in the exercise laboratory of C.U.R.I.A.Mo. and they received the indications for the correct performance of full program and exercises. In the workouts n°3, n°4 and n°25 we used isotonic machines (Lat machine, Chest Press, Leg Extension and Leg Press Technogym, Cesena, Italy) to evaluate the maximum dynamic force of extensor muscles of the leg and the flexor and extensor muscles of the arms. To estimate the 1RM we used the Brzycki 1-RM prediction equation [32]. A single test's session was composed of warm up period and (at least) 10 repetitions for each exercise, using the load/resistance detected during the familiarization session. The resistance was progressively increased until the subjects could perform 12 or fewer repetitions, for each exercise, in order to carry out the test correctly. Maximum oxygen consumption (VO_2max) was estimated through the Rockport fitness walking test, one of the most tests used to estimate VO_2max in sedentary people and a valid predictor of VO_2max [33].

Table 3. Selected data of study participants.

All							Women							Man						
BP	Patol	BMI	n	Age			BP	Patol	BMI	n	Age			BP	Patol	BMI	n	Age		
				Median	Min	Max					Median	Min	Max					Median	Min	Max
Normo	Obesity	Norm	1	56.0	56	56	Normo	Obesity	Norm	1	56.0	56	56	Normo	Obesity	Norm	0	/	/	/
		Over	12	47.0	19	68			Over	8	45.0	19	59			Over	4	61.5	32	68
		Ob	67	38.0	18	61			Ob	56	38.0	18	61			Ob	11	37.0	18	60
		Total	80	38.0	18	68			Total	65	38.0	18	61			Total	15	37.0	18	68
	Diabetes	Norm	1	54.0	54	54		Diabetes	Norm	0	/	/	/		Diabetes	Norm	1	54.0	54	54
		Over	3	61.0	45	67			Over	1	45.0	45	45			Over	2	64.0	61	67
		Ob	5	47.0	41	66			Ob	4	56.0	41	66			Ob	1	44.0	44	44
		Total	9	54.0	41	67			Total	5	47.0	41	66			Total	4	57.5	44	67
	All	Norm	2	55.0	54	56		All	Norm	1	56.0	56	56		All	Norm	1	54.0	54	54
		Over	15	47.0	19	68			Over	9	45.0	19	59			Over	6	62.0	32	68
		Ob	72	38.0	18	66			Ob	60	38.5	18	66			Ob	12	37.0	18	60
		Total	89	40.0	18	68			Total	70	39.5	18	66			Total	19	44.0	18	68
Hyper	Obesity	Norm	2	48.0	46	50	Hyper	Obesity	Norm	1	50.0	50	50	Hyper	Obesity	Norm	1	46.0	46	46
		Over	21	55.0	39	73			Over	15	60.0	39	73			Over	6	54.5	50	65
		Ob	150	51.0	19	74			Ob	88	51.0	19	74			Ob	62	51.0	25	70
		Total	173	51.0	19	74			Total	104	51.5	19	74			Total	69	51.0	25	70
	Diabetes	Norm	6	59.0	40	70		Diabetes	Norm	2	49.0	40	58		Diabetes	Norm	4	61.5	55	70
		Over	38	59.5	46	75			Over	18	59.0	51	71			Over	20	60.0	46	75
		Ob	72	58.0	33	71			Ob	32	59.0	35	71			Ob	40	57.0	33	68
		Total	116	58.5	33	75			Total	52	59.0	35	71			Total	64	58.0	33	75
	All	Norm	8	56.5	40	70		All	Norm	3	50.0	40	58		All	Norm	5	60.0	46	70
		Over	59	59.0	39	75			Over	33	59.0	39	73			Over	26	59.0	46	75
		Ob	222	53.0	19	74			Ob	120	53.0	19	74			Ob	102	53.5	25	70
		Total	289	55.0	19	75			Total	156	55.0	19	74			Total	133	55.0	25	75

During this test we indicate to patient to walk for a mile as quickly as possible. The following equation was used to predict the VO_2max estimated values:

$$VO_2\ max\ (ml/Kg/min) = 132.853 - (0.0769 \times weight\ in\ kg) - (0.3877 \times age\ in\ years) + (6.315 \times gender) - 188\ (3.2649 \times total\ time\ in\ minutes) - (0.1565 \times final\ heart\ rate).$$

Flexibility was evaluated through a bending test called *Sit & Reach* [34], conducted both in horizontal (HB) and vertical position (VB).

Statistical Analysis

Evaluation of normality was conducted using Kolmogorov - Smirnov test to assess the normal distribution of data. At first non-normally distributed variables were transformed using Box-Cox transformation, to better approximate the Gaussian distribution. Due to their asymmetry data are shown as median (min/max). An independent samples T-Test was performed to evaluate if two studied subgroups (normo- and hypertensive subjects) presented differences at baseline. A Student T-test for paired sample was used to compare all measures (anthropometry, BP and exercise program) before and after treatment (T0 vs. T4), in whole sample and in the two subgroups (normotensive and hypertensive subjects groups) according to baseline DAYBP values. $P \leq 0.05$ value was used to established statistical significance. The treatment effects value (delta changes) are obtained by subtracting the pre-exercise from the post-exercise values. A mixed model analysis of variance for repeated measures (T0,T1,T2,T3,T4) was conducted to estimate the physical activity effects on systolic SBP and DBP during (in every training step corresponding to the exercise intensity increase) and after the exercise intervention program. Furthermore, a post-hoc multiple comparison tests (tables 7 and 8) was conducted to determine which specific means differed from which others. Data extraction was conducted by graduates in Sport Science and the data was collected and extracted to Microsoft Excel spread sheets. Finally, all the analyses were performed using IBM SPSS® Statistics software package version 22.0.

Table 4. Physical activity chronic effects.

Indicator	Overall			Normo			Hyper		
	T0	T4	p	T0	T4	p	T0	T4	p
Body weight (Kg)	93.35 (55.4/150.8)	90.45 (54.7/145.6)	**	89.6 (60.5/125.50)	86.8 (58.7/124.2)	**	95.1 (55.4/150.8)	91.7 (54.7/145.6)	**
BMI (Kg/m2)	33.4 (20.6/52.3)	32.3 (20.3/49)	**	33.4 (24.2/48.8)	32.6 (23.4/48.3)	**	33.3 (20.6/52.3)	32.2 (20.3/49)	**
WC (cm)	110 (82/147)	106 (82/147)	**	108 (84/140)	103 (80/133)	**	111 (82/147)	107 (79/146)	**
WHTR (cm)	0.655 (0.47-0.85)	0.632 (0.46-0.79)	**	0.659 (0.49-0.83)	0.623 (0.46-0.78)	**	0.655 (0.47-0.85)	0.634 (0.46-0.79)	**
DAYSBP (mmHg)	130 (100/170)	125 (90/170)	**	120 (100/135)	117.5 (90/135)	*	140 (100/170)	130 (100/170)	**
DAYDBP (mmHg)	80 (55/110)	75 (50/110)	**	75 (55/80)	70 (50/90)	*	85 (60/110)	80 (50/110)	**
SBPPRE	133 (99/198)	128.5 (102/174.5)	**	126 (99/160)	122.5 (102/151)	NS	136 (103/198)	131.4 (102/174.5)	**
SBPPOST	125 (89/186)	120 (94/168.7)	**	122 (98/149)	118 (95/140)	**	126 (89/186)	121 (94/168.7)	**
DBPPRE	84 (54/116)	81 (60.5/116.7)	**	81 (58/105)	79.5 (62.3/98.5)	**	85 (54/116)	81.5 (60.5/116.7)	**
DBPPOST	80 (53/115)	77 (59/104.3)	**	78 (53/97)	76 (59.3/93.5)	**	81 (57/115)	77.4 (59/104.3)	**
VB (cm)	-8 (-39/23)	-4 (-37/38)	**	-6 (-33/16)	-3.5 (-27/37)	**	-9 (-39/23)	-5 (-37/38)	**
HB (cm)	27 (-23/54)	30 (3/54)	**	30.5 (-3/54)	33 (4/53)	**	26 (-23/49)	29 (3/54)	**
LAT (Kg)	36.3 (18.6/95.4)	46 (25.7/90)	**	36 (18.6/57.6)	45 (27.5/76.7)	**	37.15 (18.6/95.4)	46.7 (25.7/90)	**
CHEST (Kg)	26.3 (10/64.8)	36 (14.5/80.7)	**	24.8 (10/50.4)	34.1 (21.6/61.2)	**	26.85 (10/64.8)	37.2 (14.5/80.7)	**
Leg Press (Kg)	158.5 (80/300.5)	194.2 (102.9/346.8)	**	149 (86.9/295.1)	192.45 (111.1/298)	**	158.5 (80/300.5)	194.5 (102.9/346.8)	**
Leg Ext (Kg)	28.8 (11.6/86.4)	43.5 (18.5/103.4)	**	30 (14.4/57.6)	47.8 (27.7/79.2)	**	28.8 (11.6/86.4)	43.3 (18.5/103.4)	**
VO_2MAX (mm/Kg/min)	19.65 (5/43.9)	26.9 (4.8/49.7)	**	22.9 (5/43.9)	29.4 (10.9/49.7)	**	18.5 (5/42.3)	25.7 (4.8/47.7)	**

Anthropometric and physical exercise data at baseline (T0) and after three months (T4) of intensive lifestyle program in all sample, Normotensive and Hypertensive groups. Data are expressed as median (min/max). Statistical significance was considered: *=p<0.05 ,**=p<0.01, N.S.=p>0.05. Normo= Normotensive group; Hyper=Hypertensive group; BMI=Body Mass Index; WC=waist circumference; WHTR=waist-height ratio value; DAYSBP=daytime ambulatory systolic blood pressure value; DAYDBP=daytime ambulatory diastolic blood pressure value; SBPPRE= Systolic Blood Pressure values PRE-exercise; SBPPOST=Systolic Blood Pressure values POST-exercise; DBPPRE=Diastolic Blood Pressure values PRE-exercise; DBPPOST= Diastolic Blood Pressure values POST-exercise; VB=Sit & Reach test value in vertical position; HB=Sit & Reach test value in horizontal position; LAT= Lat Machine test value; CHEST=Chest press test value; Leg Press=leg press test value; Leg Ext=leg extension test value; VO_2MAX= maximum rate of Oxygen (O_2) consumption.

Table 5. Systolic Blood Pressure (SBP) values, PRE-and POST-exercise, at baseline (T0), every three weeks (T1, T2, T3) and at the end (T4) of intensive exercise program.

Time	Variable	All			Normo			Hyper		
		median	min	max	median	min	max	median	min	max
0	SBP PRE	133	99	198	126	99	160	136	103	198
	SBP POST	125	89	186	122	98	149	126	89	186
1	SBP PRE	132	102	194	124	105.7	155.5	134	102	194
	SBP POST	123	84.5	179	122	94	150	123	84.5	179
2	SBP PRE	130.85	96.7	186.5	123	96.7	151	133.7	102.3	186.5
	SBP POST	120.7	87	170.3	117.3	87	141.7	121.4	91.7	170.3
3	SBP PRE	129.6	95	190	124	102	151	132	95	190
	SBP POST	120	89	170	118.3	95.3	146	120.5	89	170
4	SBP PRE	128.5	102	174.5	122.5	102	151	131.4	102	174.5
	SBP POST	120	94	168.7	118	95	140	121	94	168.7

Value are shown for all sample, normotensive and hypertensive groups. Data are expressed as median, minimum and maximum.

Table 6. Diastolic Blood Pressure (SBP) values, PRE- and POST- exercise, at baseline (T0), every three weeks (T1, T2, T3) and at the end (T4) of intensive exercise program.

Time	Variable	All			Normo			Hyper		
		median	min	max	median	min	max	median	min	max
0	DBP PRE	84	54	116	81	58	105	85	54	116
	DBP POST	80	53	115	78	53	97	81	57	115
1	DBP PRE	83	57.5	113	80	63	99.5	84	57.5	113
	DBP POST	78.5	58	107.5	78	63	93.7	79	58	107.5
2	DBP PRE	82	59.5	111.7	79.3	65	99	82.3	59.5	111.7
	DBP POST	78	56	107	76.7	56	93.3	78	58.7	107
3	DBP PRE	80.5	59	113	78.7	63.3	94	81	59	113
	DBP POST	76.3	56	106	76	60.3	91.7	76.3	56	106
4	DBP PRE	81	60.5	116.7	79.5	62.3	98.5	81.85	60.5	116.7
	DBP POST	77	59	104.3	76	59.3	93.5	77.4	59	104.3

Value are shown for all sample, normotensive and hypertensive groups. Data are expressed as median, minimum and maximum.

Table 7. Post hoc analysis of systolic blood pressure (SBP) post-exercise.

Time		SBP POST Normo (mmHg)		SBP POST Hyper (mmHg)	
		Mean Diff	p	Mean Diff	p
0	1	0,1	NS	2,3	**
	2	3,1	**	3,6	**
	3	2,9	*	4,9	**
	4	3,2	**	4,9	**
1	0	-0,1	NS	-2,3	**
	2	3,1	*	1,3	NS
	3	2,9	*	2,6	**
	4	3,2	*	2,6	**
2	0	-3,1	**	-3,6	**
	1	-3,1	*	-1,3	NS
	3	-0,2	NS	1,3	*
	4	0,1	NS	1,3	NS
3	0	-2,9	*	-4,9	**
	1	-2,9	*	-2,6	**
	2	0,2	NS	-1,3	NS
	4	0,3	NS	0,0	NS
4	0	-3,2	**	-4,9	**
	1	-3,2	*	-2,6	**
	2	-0,1	NS	-1,3	NS
	3	-0,3	NS	0,0	NS

Table 8. Post hoc analysis of diastolic blood pressure (DBP) post-exercise.

Time		DBP POST Normo (mmHg)		DBP POST Hyper (mmHg)	
		Mean Diff	p	Mean Diff	p
0	1	-0,2	NS	1,1	*
	2	1,0	NS	1,9	**
	3	2,5	**	3,5	**
	4	1,8	NS	3,5	**
1	0	0,2	NS	-1,1	*
	2	1,2	NS	0,7	NS
	3	2,7	**	2,3	**
	4	2,0	**	2,4	**
2	0	-1,0	NS	-1,9	**
	1	-1,2	NS	-0,7	NS
	3	1,5	*	1,6	**
	4	0,8	NS	1,7	**
3	0	-2,5	**	-3,5	**
	1	-2,7	**	-2,3	**
	2	-1,5	*	-1,6	**
	4	-0,7	NS	0,1	NS
4	0	-1,8	NS	-3,5	**
	1	-2,0	**	-2,4	**
	2	-0,8	NS	-1,7	**
	3	0,7	NS	-0,1	NS

Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) values POST exercise. Statistical significance was considered: *=p<0.05, **=p<0.01, NS=p>0.05. Notes: Mean Diff = mean difference; Normo= Normotensive group; Hyper=Hypertensive group.

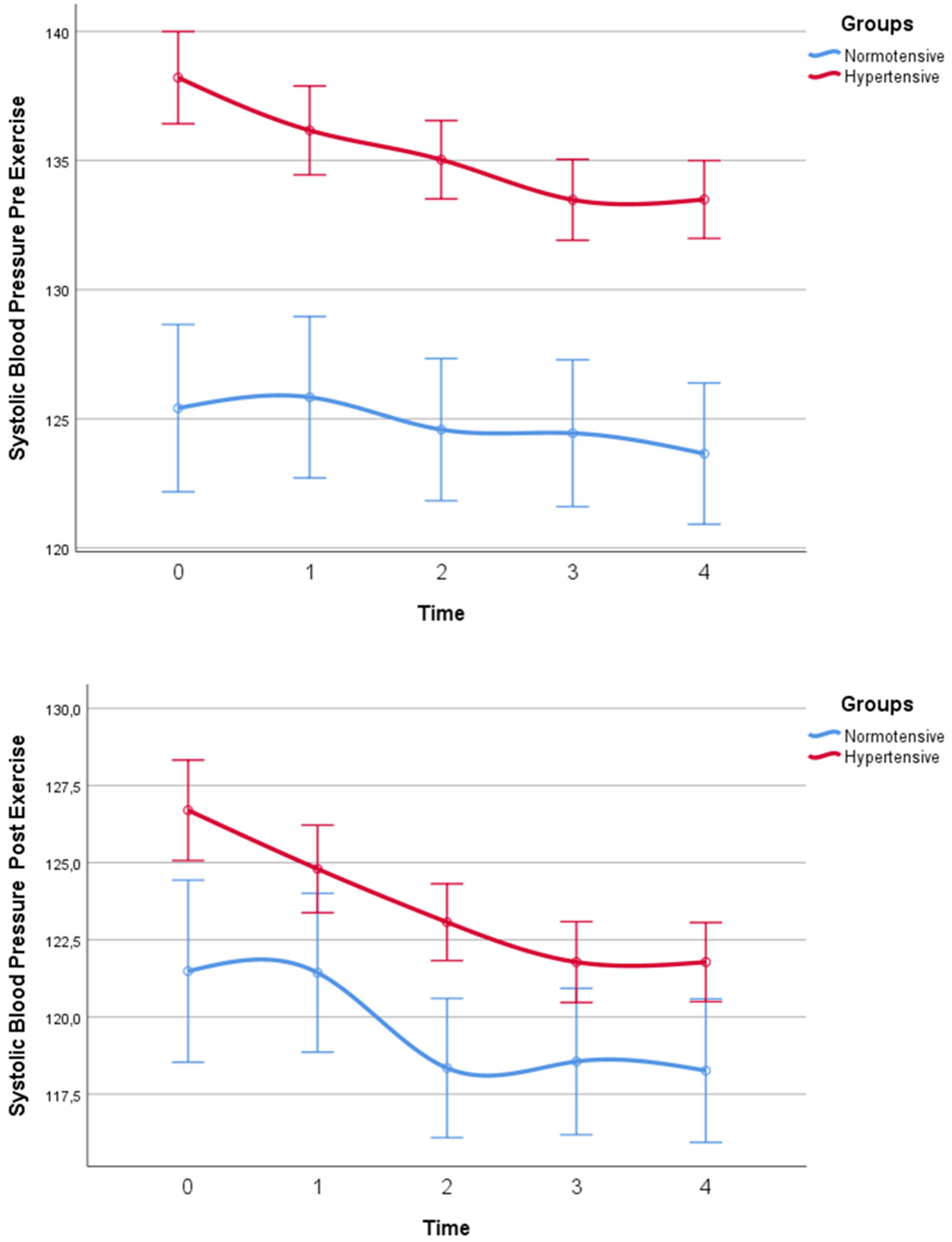

Figure 1. Systolic Blood Pressure mean values before (upper panel) and after (bottom panel) exercise sessions.

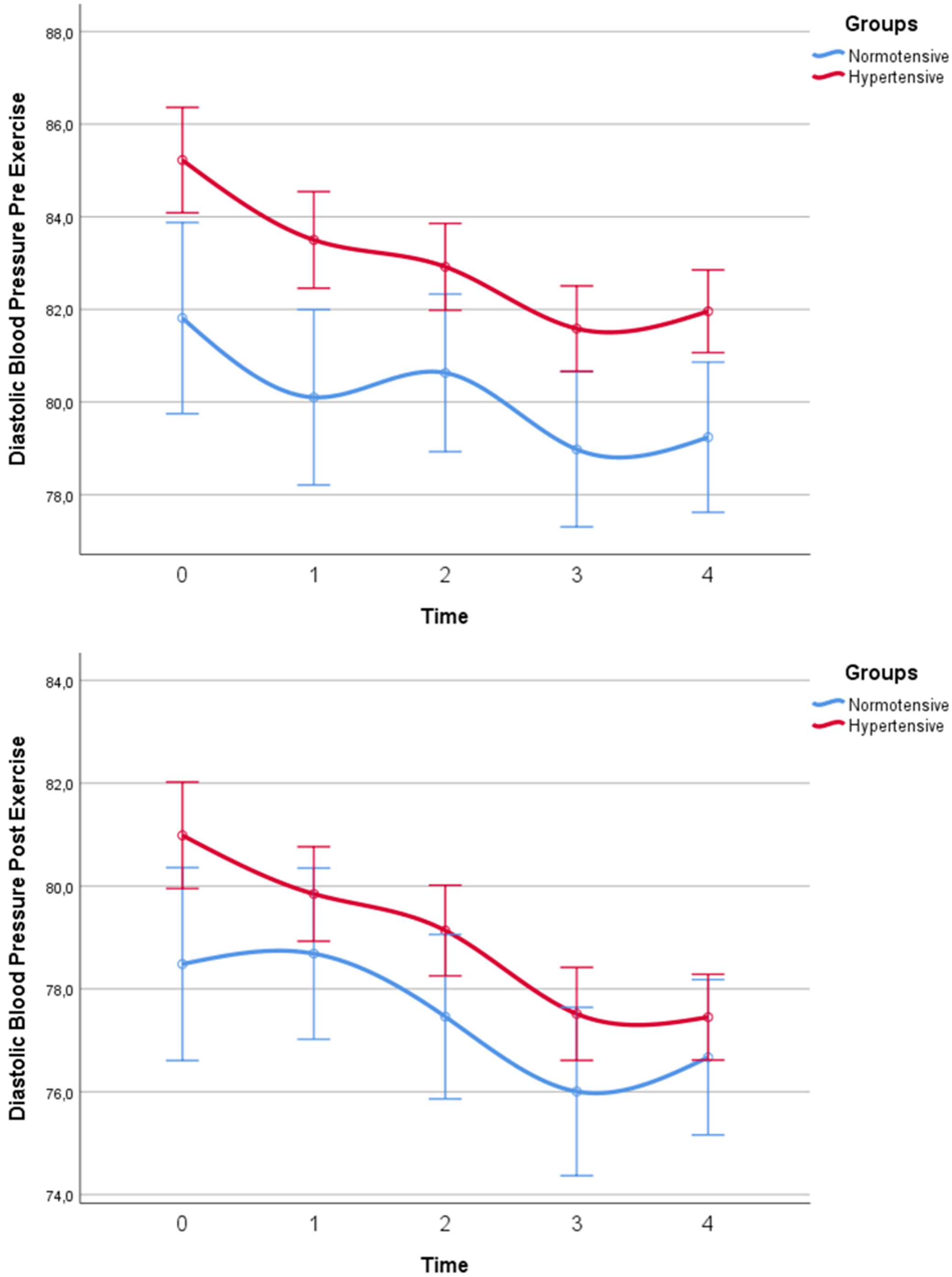

Figure 2. Diastolic Blood Pressure mean values before (upper panel) and after (bottom panel) exercise sessions.

RESULTS

At the end of the intervention period (T4), in all subjects anthropometric parameters such as body weight, BMI, WC, WHTR index significantly improved as compared to baseline (Table 4). Similarly, physical exercise measures such as flexibility (both in vertical and horizontal position), maximum dynamic muscle strength of upper (Lat machine, or LAT; chest press, or CHEST) and lower limbs (LEG PRESS and leg extension, or LEG EXT) and VO_2 max showed a statistically significant

(p<0.01) improvement. Finally, DAYSBP and DAYDBP as well as BP values PRE- and POST-exercise significantly decreased at the end of the intervention period as compared to baseline. No statistically significant difference was found between males and females in all variables (data not shown).
The improvement of the anthropometric and exercise parameters observed at T4 in the whole group was also observed when subjects were split in normotensive and hypertensive groups. In particular, with regard to BP data, the comparison of data between normotensive and hypertensive groups indicated that, with the exception of SBPPRE in the normotensive group, DAYBP, DAYDBP, DBPPRE, DBPPOST and SBPPRE significantly decreased at T4. In fact, the average DAYSBP decrease was of 10 mmHg in the hypertensive subjects and 2.5 mmHg in the normotensive subjects, respectively. The DAYDBP drop was of 5 mmHg in both groups.

The repeated measures analysis of variance with a within subjects factor (time) and between subjects factor (group) showed that BP values measured in the gym during physical activity sessions decreased significantly during the exercise treatment period, both in the normotensive and hypertensive groups, although to a greater extent in the hypertensive group, confirming the result obtained from the analysis of the whole sample. Therefore, exercise-related effects on BP were observed over the 3-month intervention period within subjects (p<0.0001), with no difference between groups (p>0.05).

In the whole group, post-exercise SBP and DBP decreased form baseline to T4 by 5 mmHg (from 125 to 120 mmHg) and by 3 mmHg (from 80 to 77 mmHg), respectively, after the training period (Tables 5 and 6). Between group comparisons indicated that, in the hypertensive subjects, post-exercise SBP and DBP values decreased (5.0 and 3.6 mmHg, respectively) more than those in the normotensive group (4.0 and 2.0 mmHg, respectively). Overall, in the normotensive group, the drop in BP was mainly evident in the 2nd and the 4th training period, whereas in the hypertensive group the decrease in BP values was more continuous from baseline to T4 with a greater drop in the second training period (fig. 1 and 2). BP values showed a statistically significant decrease in DAYSBP and DAYDBP, as well as in BP values PRE- and POST-exercise.

DISCUSSION

The main aim of the study was to establish whether a lifestyle intervention based on the combination of diet, increased physical activity, and behaviour modification [30] might have improved health-related variables, particularly blood pressure, in overweight/obese adult subjects. Among the participants at C.U.R.I.A.Mo. trial, we recruited 378 people with overweight/obesity and/or type 2 diabetes, allocated to normotensive or hypertensive groups, to take part in a multidisciplinary intervention including physical exercise sessions. The results demonstrate that a three-month period lifestyle multidisciplinary intervention is associated with a significant improvement in CV risk factor such as reduction in BMI, WC, WHTR index and BP values. In addition, it is worth pointing out that the improvement in BP values started to become evident after only a few weeks into the intervention. To the best of our knowledge, the present study is the first structured lifestyle multidisciplinary intervention involving people with obesity and/or type 2 diabetes, focused on physical exercise-induced effects on BP. Wang et al. [35] found similar results in overweight women following 10 weeks of supervised exercise training. In our study, we observed an initial BP decrease after only three weeks (T1, Figure 1 and Figure 2), both in normotensive and hypertensive subjects with overweight/obesity.

Cardoso et al. have reviewed the current literature on the acute and chronic effects of aerobic and resistance exercise on ambulatory blood pressure in normotensive and hypertensive subjects and found that a single episode of aerobic exercise reduces ambulatory blood pressure in hypertensive patients. They also pointed out that blood pressure levels decrease soon after exercise in comparison to blood pressure measured before exercise or on a control day when no exercise is performed [14]. However, to be clinically relevant, the reduction of BP after exercise must have a considerable effect and must be maintained for a long period of time under ambulatory conditions. In the present study, post-exercise SBP and DBP decreased and remained lower than pre-exercise measurements up to the end of the three-month period of observation (T4). Other studies of the C.U.R.I.A.Mo. research group have shown that BP reductions observed at three-months in daytime ambulatory SBP and DBP in BP can be maintained over a two-year follow-up visits, provided the lifestyle changes of the multidisciplinary intervention are maintained [10].

It is known that a clinically meaningful BP reduction, as used in many hypertension trials, is arbitrarily defined as an absolute SBP and DBP reduction of 3 mmHg or more because this significantly reduces the incidence of CVD in both hypertensive and normotensive individuals [36]. Hess et al. reported that after 6 weeks of isometric training exercise, reductions in SBP were similar to the antihypertensive effects observed in monotherapy of 5-7 mm Hg [37]. In the present study we observed BP value reductions after three weeks (T1) of exercise. Furthermore, as shown in tables 3a and 3b, BP values were positively affected by every single session of mixed type exercise (reduction of PRE-POST exercise of systolic and diastolic pressure values). Considering that a single training period of the type presented may cause a sustained decrease of BP (acute effect) that lasts for a few hours after training, it is strongly recommended to exercise several times a week (better if daily). Based on these results we can conclude that just four sessions of supervised exercise (twice a week) are enough to begin to get benefits on BP value reductions both in "normotensive" and "hypertensive" people.

According to Martinez Aguirre-Betolaza et al. [13] better BP improvements in overweight/obese people with hypertension are achieved when the exercise training is individually designed and supervised, empowering the existing exercise recommendations. In that context, the results of the present study are in line with those of Martinez Aguirre-Betolaza et al. [13], and contributes to scientific evidence by using a specific multidisciplinary clinical program, including a structured exercise program individualized for type, frequency and intensity in order to effectively counteract hypertension and overweight/obesity. In addition, exercise was supervised by exercise physiologists with an Exercise Sport Science degree and endocrinologists. For that reason, the present study may not be replicable in a simple ambulatory counselling setting aimed at increasing regular exercise if devoid of specific instrument, machines, and especially a team of highly qualified personnel including graduates in Sport Science [38,39].

The mechanisms responsible for BP reduction in our study are not clear. However, considering that hypertension is a multifactorial disease, it is possible that different mechanisms may mediate the hypotensive effects of mixed exercise training. Among the possible mechanisms we mention a reduction of vascular resistance, in which the sympathetic nervous system and the renin-angiotensin system appear to be involved [40] as well as body weight and fat mass loss.

Despite the novelty of our results, we should acknowledge a few limitations of our study. First, the intervention included food habits, Mediterranean diet adherence and psychological and motivational interviews. However, it needs to be recognized that the relative impact of the single components of the intervention on BP values of people affected by overweight/obesity or type 2 diabetes cannot be understood from our study [41]. Generally, we believe that the exercise program (25 sessions of 90 minutes each) has played a major role in the outcomes as compared with nutritional (3 meetings of one hour each) and psychological (2 meetings of 45 minutes each) interviews. Second, despite the fact that our intervention is a multidisciplinary one, we focused in this analysis mainly on the role of supervised exercise. Third, the results of the other variables related to nutritional and psychological intervention are not reported. Finally, the study lacks a control group because this was not included in C.U.R.I.A.Mo. clinical trial.

CONCLUSION

These results demonstrate that an intensive lifestyle intervention including a regular practice of supervised exercise should be recommended for overweight/obese adults with high BP value to obtain improvements on body weight, body composition, BP value, muscular strength, flexibility and maximum oxygen consumption. Beneficial effects of exercise on BP value reductions can be seen in as little as 2 to 3 weeks after starting the exercise program. Future studies will be needed to better understand the combined effects associated with exercise, nutritional and motivational counselling on blood pressure in people affected by overweight/obesity or type 2 diabetes.

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