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CARDIOVASCULAR, METABOLIC AND BODY COMPOSITION CHANGES DUE TO TWO DIFFERENT TYPE OF PHYSICAL ACTIVITY IN OBESE AND/OR HYPERTENSIVE ADOLESCENTS: A PROSPECTIVE COHORT STUDY

CANDIDATE: Federico Abate Daga

SUPERVISOR: Ch.mo Prof. Franco Veglio

DOCTORAL SCHOOL COORDINATOR: Ch.mo Prof. Franco Veglio

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DECLARATION OF AUTHORSHIP

I, Federico Abate Daga, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis. I have used data acquired by Professor Veglio's staff and by myself in Molinette Hospital (AOU Città della Salute, Turin, Italy) and in the laboratory of Adapted Training and Performance of the University of Turin.

Federico Abate Daga

ABSTRACT

INTRODUCTION: It has been demonstrated that obesity in childhood and adolescence may lead to cardiovascular and metabolic alterations and early onset of organ damage. In addition, obesity can generate low-grade chronic inflammation, body composition modifications and increasing the risk of metabolic or cardiovascular diseases. Physical activity has been recognized as the best and most economic method to manage obesity and to prevent cardiovascular and metabolic diseases. However, it is still not clear what kind of physical activity can be considered as the most suitable to face obesity. Thus, the aim of this study was to assess the effects of 24 weeks of resistance versus combined training on cardiovascular and metabolic profile and body composition in obese adolescents. **METHODS**: 31 adolescents with moderate to severe obesity were enrolled for this study. Cardiovascular system was evaluated monitoring heart rate variability (HRV) through a 20-minute electrocardiography, ABPM over the course of 24-h and PWV. Metabolic profile was asses analysing a blood sample. In addition, body composition was evaluated using BIA-ACC medical device (Biotekna, Italy). All measurements were assessed after recruitment (T0). Then, participants were randomly assigned to either resistance (RT) or combined (CT) training. All assessments were re-evaluated after 24 weeks (T1) of low to moderate-intensity training. Body compositions were evaluated again after 12 weeks of detraining (FU). **RESULTS**: The mean age was 15.5 ±1.55 years, BMI 33.3±5.1 kg/m2, (prevalence of male 43.8%, prevalence of clinic hypertension 18.8%). It was observed in both groups a significant decrease in office diastolic blood pressure (DBP) (75 ± 7.2 vs. 68 ± 6.9 mmHg, $p<0.01$) and heart rate (HR) (84 ± 17.1 vs. 74 ± 10.4 bpm, $p<0.05$). Metabolic profile showed a significant change in triglycerides ($p< 0.05$) and a trend to improvement in values of HDL ($p=0.067$) and blood sugar ($p=0.075$) in both groups. For that it concerns body composition, Fat Mass, AAT and IMAT were significantly reduced after 24 weeks of training (T1) in both groups ($p< 0.05$), while TBW, FFM, RMR and body density increased significantly ($p<0.01$). Bone Mass, T-score, Muscle Mass and S-Score were increased just in RT ($p< 0,01$) while BMI were reduced only in CT ($p<0.05$). After 12 weeks of detraining, values of TBW, FFM, FM, BMR, AAT and AT are significantly regressed ($p<0.01$). **CONCLUSION:** Both RT and CT produced benefits on obese adolescents. However, resistance training provided improvements of muscle and bone revealing more efficient in modify body composition. For this reason, RT should be considered in the management of obesity in adolescence.

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FREQUENTLY USED ABBREVIATIONS
(body composition)

BMI	*Body Mass Index*
TBW	*Total Body Water*
FFM	*Fat Free Mass*
FM	*Fat Mass*
BMR	*Basal Metabolic Rate*
AT	*Adipose Tissue*
AAT	*Abdominal Adipose Tissue*
IMAT	*Inta Muscolar Adipose Tissue*

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INTRODUCTION

Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health. As a matter of fact, obese patients have greater chances to develop many medical problems, including cardiovascular diseases, diabetes mellitus type 2, obstructive sleep apnea, certain types of cancer, osteoarthritis and asthma [1]–[3]. The World Health Organisation (WHO) underlines as 2,8 million of People die every year because of obesity and its related diseases. In addition, it was estimated that 2.3% of the world DALY (Disability-Adjusted Life Year) is due to this condition. Consequently, because of its serious health consequences, obesity has very high costs that affect the Health Care System of many countries. Several studies [4], [5] show as 4854 million euros are spent every year in direct contrast to this disease. The amount is greater (5019 million euros) when indirect costs are considered.

Obesity: Epidemiology, Diagnosis and limits of BMI

A person has traditionally been considered obese when body weight is more than 20 percent over the ideal one. In 1997, WHO formally recognized obesity as a global epidemic [6] and in 2013 the American Medical Association classified it as disease. The causes that generate this medical condition are complex and multifactorial. First of all, genetics and individual behaviours such as incorrect diet, sedentary life style and lack of sleep during night-time (the so called "social jetlag"[7]) are considered very important risk factors [8]. Furthermore, level of educations, socio-economic status and life environment play an important role in onset of obesity [9]. According to several studies [9]–[11], people from lowest social levels of our industrialized society show lower levels of education, a trend to consume more junk food, to adopt bad behaviour and, consequently, to be more exposed to the risk of being obese. Furthermore, electronical devices and very urbanized areas provides lots of chances to be active and awake during the night. Nevertheless, our "internal clock" regulates energy consumption and distribution following a circadian rhythm and controls the sleep timing through the process of entrainment [12]. Thus, its destruction due to bad behaviours and a lifestyle "against the clock" increases obesity outbreak [7].

Regardless of the reasons which led to its onset, obesity is a medical problem and it should be diagnosed as any other pathology. The most common methods to identify obesity is to calculate the Body Mass Index (BMI) of a person. BMI is a value derived from the person's weight and height. It is identified as the body weight divided by the square of the body height. It is universally expressed in metrics units where mass is conveyed in

Kilograms and height in meters (Kg/m^2). According to WHO, a person with a BMI greater than or equal to 30 kg/m^2 is considered obese. When BMI is over the value of 30 kg/m^2 three grade of obesity are identified: grade 1 (BMI 30·0–<35·0 kg/m^2), grade 2 (35·0–<40·0 kg/m^2) and grade 3 (40·0–<60·0 kg/m^2). On the other hand, normality is considered when BMI is from 18.5 to 25 kg/m^2, overweight from 25 to 30 kg/m^2 and underweight <18.5 kg/m^2. These data are summarized in table 1.

Values of BMI*	
Underweight	<18.5 kg/m^2
Normal weight	18.5 to 25 kg/m^2
Overweight	25 to 30 kg/m^2
Obese	>30 kg/m^2
Obese Grade I	**30·0–<35·0 kg/m^2**
Obese Grade II	**35·0–<40·0 kg/m^2**
Obese Grade III	**40·0–<60·0 kg/m^2**

WHO. Obesity and overweight. Fact sheet N°311. Geneva: World Health Organization, 2015

Table 1. Categories of body weight according to BMI values.

For that it concerns children and adolescent, a better strategy is to consider BMI normalized for age and calculated in percentiles. Children are considered obese if their BMI is –<95th percentile given by the Centres for Disease Control and Prevention [CDC] ad overweight if it is from 85th to 95th percentile. This classification seems to be valid as an indicator of body fatness and risk children and adolescents [13].

High values of BMI are strictly related to all causes of mortality in all over the world. In a meta-analysis of 239 prospective studies leaded in four continents, Di Angelantonio et colleagues [14] underline as this relation is broadly consistent independently from the ethnical diversity of the investigated populations. Therefore, BMI seems to be a good and simple way to diagnose overweight and obesity, in particular in children and sedentary people[13], [15] As explained before, BMI is a number that represents the relationship between a person's height and weight. BMI was created as a tool that people could use to determine whether they were too heavy for their height. Unfortunately, it has begun a sort of "fat-meter" able to identify how fat a person is. However, body weight represents the sum of all body components (organs, tissues, bone, muscles etc.), not only the expression of body fat. Whether BMI can effectively neutralize the influence of height on body weight, it provides no distinction between Fat Mass (FM) and body Free Fat Mass (FFM) [16]. People with very developed muscles mass such as athletes can show high levels of BMI due to their muscle weight and not because they have an excess of fat [17]. Consequently, certain types of population such as athletes or very active people cannot be evaluated only on BMI values. It is recommended to identify the amount of fat percentage using secondary tools as skinfold [18] or body composition analysis [19]. On the other hand, BMI can be not so suitable in other situations. Patients with metabolic dysregulation, organ damage due to a persistent inflammatory status, inflammatory chronic disease, chronic stress etc., may present a normal BMI, but very low levels of bone and muscles if their body composition is analysed [20]. This condition can create an important impairment in bone-muscle-fat ratio, leading to a new form of obesity, the so-called Osteo Sarcopenic Obesity (OSO) [21]. OSO will be discussed later in this essay.

Finally, BMI is a useful tool that provides a general idea about a person's health status. it is a simple, quick to calculate and not expensive at all. However, BMI does not completely inform about people's individual weight and health risks. Thus, further evaluations are needed to better investigate obesity epidemic.

Obesity and body composition

As previously discussed, further investigations are needed to better diagnose obesity. One way to accomplish it is to analyse the body composition.

Body composition describes how the human body is made of. This method provides objective data that is unobtainable from scale weight alone and describe the health status better than BMI because it can differentiate between fat, protein, minerals, and body water, more simply between fat mass (FM) and fat-free mass (FFM) [22].

In the last decades, the interest about body composition is increased together with scientific researches on this matter and new evaluation methods in this field. Wang et al [23] proposed a five-level model for body composition research. In this representation, authors purposed 5 compartments in which body composition can be investigated: Atomic level, Molecular level, Cellular level, Tissue-organ level, Whole-body level. Each level can be analysed separately with different methods, but all are interconnected and work together as a “whole body”[23]. The first one, the atomic level represents the essential building blocks of the human body, that are atoms or elements. About 50 elements of the 106 discovered where identified in our body. The most represented are 6: oxygen, carbon, hydrogen, nitrogen, calcium and phosphorus. They account for 98% of the total elements and, the 60% of this amount is constitute by oxygen. [24].

The second level is the Molecular level, that involves how the elements are organized to build molecules and components. The majors are water, lipid, protein, mineral and glycogen. Here, a special mention goes to lipids (that are extremely involved in the epidemic of obesity). Among the principal components of this level, lipid is the most confusing because the term lipid and fat are usually confounded and wrongly utilized. Lipids are defined as a group of chemical compounds that are insoluble in water and very soluble in organic solvents such as diethyl ether, benzene and chloroform [25]. In human body were recognized about 50 different lipids that where divided according to their organic chemistry into five subcategories: simple lipids (including triglycerides and waxes), compound lipids (phospholipids and sphingolipids), steroids, fatty acids and terpenes [25]. The term fat is synonymous of triglyceride; therefore, it can be affirmed that fat is a subcategory of lipids (the first one: simple lipids). Furthermore, lipids can also be classified as essential (Le) and non-essential (Ln). Essential lipids (eg. sphingomyelin and phospholipids) serve very important functions such as forming cell membranes while non-essential lipids (mostly triglyceride) fulfil other function as thermic isolation and “fuel” storage. Commonly, about 10% of total body lipid is essential and 90% non-essential [23] [25].

The Cellular level is the third one. It comes from the seconds where molecules conglomerate together to form cells. The coordination and interactions among the function of different cells are the core of the study of human physiology both in health and disease [23]. In addition, this level is an important area in body composition research. Cellular level is characterized of three main components: cells, extracellular fluid and extracellular solid.

The fourth level is the so-called Tissue-system. Cell, extracellular fluid and solid conglomerate together to form organs, tissues and system. It is also particularly important because in this level tissues and organs such as adipose tissue, bone and muscle mass are investigated. Especially, in these last years it is possible to easily investigate this organs and tissues thanks to new bio-impedance devices able to provide a valid overlook on organs and tissues health status [26]. System is related to the co-operation of several organs (an example of system is the cardiovascular system with blood, hearth and vessels working together).

Finally, the fifth level contemplates the Whole-body. It concerns body size, shape and exterior physical characteristics. Ten dimensions are identified at this level: stature, segments length, body breadths, circumferences, skinfold thicknesses, body surface area (BSA), body volume, Bwt (head weight + neck weight + trunk weight), Body Mass Index (BMI) and body density[23], [27]. These parameters are also part of what it is called "anthropometrics".

Body composition can be analysed using many techniques, depending of the which level it would be investigated. The cheapest and easiest is measuring the Whole-body by recording anthropometrics. Body composition is evaluated recording some anthropometric parameters such as height, weight, circumferences, skinfolds (etc…). After data collection, equations and predictive models provide an overview of how the body is made of [18], [28]. However, even if it is considered valid, the analysis only of the Whole-body level can present a lack of information in the assessment of body composition. It is necessary to improve data through other methods able to investigate the problem at a molecular, cellular or tissue-system level.

Dual-Energy X-Ray Absorptiometry (DXA) is often considered one of the most accurate methods of body composition analysis [19]. It is based on a three-compartment model that measures bone mineral content, FM and FFM. It uses a very small dose of ionizing radiation to produce pictures of the inside of the body. Measurement protocol of a full body DXA involves the individual lying on the device open scanner for approximately 8 minutes. During this time, the 'arm' of the machine moves over the length of the body, and scanning using two x-ray beams. The more energy that is absorbed, the denser is the tissue. Two energies are used to allow estimates of soft tissue absorption, separate to bone [29]. The DXA also provide segmental body composition analysis and it is considered the gold standard measurement tool for the diagnosis of osteopenia and osteoporosis [30]. Although it is often considered one of the most accurate methods of body composition analysis, it shows limitations as well. Measurements on athletes or very trained people may be affected by muscle glycogen levels, hydration status and changes in muscle metabolites such as creatine [31]. This may lead to a misrepresentation of FFM, influencing estimates of body composition made with DXA. In addition, DXA could not be performed if the person's weight is higher that the machine table limit. Consequently, extreme obese people may not be evaluated with DXA [32].

Finally, an attractive option for body composition analysis has increased its popularity, particularly in epidemiological research. It is the Bioelectrical Impedance Analysis (BIA). Thanks to the low cost, speed of measurement and lack of need for technical expertise BIA is more and more utilized in the field of body composition. BIA is based on the concept that electric current flows through the body at different rates depending on its composition [33]. It involves running a light physiological electrical current through the body and determining body composition through the resistance of the tissues to the electrical current. This provides a measure of total body water, which is converted to FFM on the assumption that 73% of the body's FFM is water [34]. BIA data is influenced by hydration status. Consequently a very severe obesity, bad lifestyle or very hard physical exercise could affect body composition analysis because of alterations in hydration status [35]. Despite this, BIA was found as a good method to asses body composition. Quick, easy, practical and accurate in determinate the Tissue-system (bone and muscle mass, adipose tissue etc.) [26].

Fat mass and its distributions in the whole body are parameters investigated by these techniques. Body fat distribution is a strong metabolic and cardiovascular risk factor [36]. Moreover, fat storage placement is extremely important in determining obesity comorbidity. In fact, a marked storage of adipose tissue in the upper body (abdominal region) is associated with the development of obesity-related comorbidities and even all-cause mortality. In contrast, accumulation of fat in the lower body (gluteofemoral region) seems to provide a protective lipid and glucose profile together with a decrease in cardiovascular and metabolic disease prevalence [37], [38]. Considering this, information about Abdominal Adipose Tissue (AAT), visceral fat or Intra Muscolar Adipose Tissue (IMAT) can be very useful to manage obesity and its related comorbidities.

Osteo Sarcopenic Obesity (OSO)

In these last years a new form of obesity was identified, the Osteo Sarcopenic Obesity (OSO). It is an emerging health problem characterized by the simultaneous manifestation of excess body fat and low muscle and bone mass. Roubenoff [39] described this condition as the confluence of the aging and the obesity epidemics. In OSO the impairment of bone, muscle and fat is associated with a low-grade chronic inflammation, caused overall by an inadequate diet and lifestyle [40]. Typically, loss in muscle and bone are associated with decreases in physical activity. When losses hit a threshold, physical activity becomes even more limited, leading to a vicious cycle of progressive loss of muscle and bone and gain in fat. Moreover, this condition represents a sort of “priority lane” for the insurgence of others serious diseases such as cancer or diabetes [41]. This condition is usually related to aging. So, it seems to be a problem of the elderly. Nevertheless, Stefanaki and colleagues [42] found a sort of *forme fruste* of OSO in youth obese. Even if they are the only group to have identified a precursor of OSO in youth, the problem should not to be underestimated considering that obesity is growing in youth population of our industrialized society.

OSO can be diagnosed only with techniques that examine the Tissue-System level. The diagnostic criteria include measurements of bone, muscle, and fat. In clinics, these criteria are usually investigated with dual energy X-ray absorptiometry (DXA) technology. However, recently the setting of some medical devices working with BIA technology are also able to provide a good diagnose of OSO.

Ilich and collegues [21] described three key factors to diagnose OSO: bone mineral density, appendicular lean mass (muscle) and fat mass.

To asses bone mineral density (BMD) T-scores $\leqslant -1.0$ standard deviation (SD) of the femoral neck, proximal femur, or lumbar spine is utilised, as recommended by the official diagnostic criteria for osteopenia/osteoporosis [43].

Appendicular lean mass (ALM) is a common measured in the diagnosis of sarcopenia [44]. Negative residuals from a linear regression model are used to identify those individuals whose amount of ALM is lower than the predicted value for their height and fat mass. The 20th percentile of the residual distribution is used as the cut-off point for sarcopenic obesity.

Finally, when fat mass values (obtained with DXA or validated BIA) are $\geqslant 32\%$ and associated with a T-scores $\leqslant -1.0$ standard deviation (SD) and a lean mass (muscle) on the 20th percentile OSO is diagnosed.

Obesity and cardiovascular diseases

Obesity has consistently been associated with an increased risk for metabolic and cardiovascular disease [45]. An excess of fat mass has a high negative impact on vessels surrounding adipose tissue and, consequently, on blood circulation that lead to heart overuse with possible risk of failure [46]. Cardiovascular risk is improved if obesity persists from childhood. Buscot and collegues in the the Cardiovascular Risk in Young Finns Study [47], showed that trends of worsening or persisting obesity were associated with an increased risk of cardiovascular disease in adulthood. On the contrary, it was found that participants who reduced their elevated childhood body mass index (BMI) to normal levels had a similar risk for dyslipidaemia and hypertension compared with those who were never obese or overweight. In another big longitudinal cohort study conducted on 67,278 subjects, half of whom where obese, Foy and collegues [48] found that participants with obesity were significantly more exposed to the risk of develop hypertension and diabetes. Moreover, eight years after the first screening, obesity was strongly associated with diagnosis of atrial fibrillation after controlling for age, gender, hypertension, and diabetes.

Recent studies show that the most common myocardial disorder in people with obesity is HFpEF, characterized by ventricular fibrosis, decreased distensibility and modestly increased cardiac volume together with relatively low natriuretic peptide levels and impaired renal function [49], [50]. HFpEF produce an higher risk of all-cause mortality when excess of fat is stored in the abdominal region (Abdominal Adipose Tissue – AAT) [51].

Furthermore, if the excess of fat may represent a problem for the cardiovascular system, the condition of obesity makes the things worse. Obesity promotes systemic inflammation, and inflammation can drive adipogenesis. Consequently, fat mass is likely to increase. Chronic systemic inflammation, along with increased accumulation of epicardial adipose tissue has been observed in people with obesity [52]. A big problem starts when atherogenic lipoproteins in the circulation become entrapped in the subendothelium. They generate an inflammatory reaction that promotes atheromatous plaque. This is the beginning of atherosclerosis [52]. In addition, it is increasingly recognized that the adiposopathic 'sick fat' surrounding the heart can also transmit inflammatory responses that promote heart disease [52]. Sequentially, a systemic inflammatory status provoked by obesity promotes the expression of a proinflammatory phenotype in epicardial fat, particularly the adipose tissue surrounding the coronary arteries. Chronic inflammation and accumulation of epicardial fat is strongly associated with the presence, severity and progression of coronary artery disease, independent of visceral adiposity [53].

Considering these dangerous consequences that an obese may have on cardiovascular system, a good monitoring of heart and vessels is necessary. Firstly, the simplest way to learn about cardiovascular system is to record blood pressure. An optimal blood pressure level is a reading under 120/80 mmHg with a tolerance up to 139/89mmHg [54]. Values that not match with this range should be considered as non-normal and need an investigation. Increased adiposity, is strongly associated with higher blood pressure and development of hypertension [55]. Wilson and colleagues in the Framingham Heart Study [56], followed participant for up to 44 years and estimated that excess body weight (including overweight and obesity) accounted for approximately 26 percent of cases of hypertension in men and 28 percent in women. In addition, Forman and colleagues [57] in the Nurses' Health Study followed a group of women up to 16 years and identified that the 40 percent of new hypertension cases were due to overweight and obesity.

Blood pressure monitoring is accomplished through several methods. Office blood pressure is usually recorded using the auscultatory or the oscillometric method. In addition, a 24-hours screening can be performed by Ambulatory Blood Pressure Monitoring over the course of 24 hours (ABPM 24 hours). The auscultatory method (also known as the Riva Rocci Korotkoff or manual method for blood pressure measurement) consists in the listening of Korotkoff sounds in the brachial artery [58]. This is considered as the gold standard for blood pressure assessment. Blood pressure is acquired using sphygmomanometer and stethoscope for listening the Korotkoff sounds. However, there are many variables that affect the accuracy of this method and numerous studies have shown that physicians and healthcare providers rarely follow the established guidelines for taking proper manual blood pressure measurements [59]. On the other hand, the oscillometric method is the measuring of the pressure variations in the blood pressure cuff caused by the oscillation of blood flow through the brachial artery. The blood pressure values are then calculated by an empirically derived algorithm. Most automated blood pressure monitors use the oscillometric method for blood pressure since is it less susceptible to external noise [60]. Finally, twenty-four-hour ambulatory blood pressure monitoring (ABPM 24 hours) is a way of measuring blood pressure and monitoring and managing hypertension. ABPM 24 hours allows many blood pressure readings to be recorded over a 24-hour period, whether the patient is awake or asleep. In most cases, with ABPM, readings are recorded every 20 to 30 minutes during the day and every hour at night. In addition, the heart rate can also be measured at the same time. With this methods, multiple blood pressure readings can be averaged over the 24-hour period to obtain the mean or average blood pressure. Furthermore, variations in blood pressure, heart rate, blood pressure distribution pattern, and other statistics can be calculated. Recent findings [61] show that ABPM more accurately reflect the risk of cardiovascular events respect of office measurements of blood pressure. In addition. It can better recognized white coat, masked and sustained hypertension [62].

Another way to investigate cardiovascular system health is to calculate the Pulse Wave Velocity. Pulse Wave Velocity (PWV) is a measure of arterial stiffness, or the rate at which pressure waves move down the vessel. Arterial stiffness is an independent risk factor for cardiovascular disease [63]–[66] and has been suggested as a marker of vascular aging [67]. The main structural changes in the vessel wall leading to arterial stiffness are degradation of elastic fibres and replacement with collagen fibres leading to arteriosclerosis [68].

PWV is considered the gold standard for arterial stiffness assessment [69], [70]. Arterial stiffness has been recognized as an indicator of target organ damage and has been established as a highly reliable prognostic parameter for cardiovascular morbidity and mortality in a variety population including obesity, diabetes and hypertension [71], [72]. Obese people shows an altered arterial stiffness that is visible since childhood and adolescence [73].

Non-invasive assessment of PWV can be performed using magnetic resonance imaging, vascular ultrasound, echotracking, mechanotransducers and tonometric devices [74]. Generally, these devices determine the time elapsed between two pressure wave forms from two different anatomical sites, usually between carotid and femoral artery sites. The travel distance used to calculate velocity is normally taken from body surface landmarks on the subject. Although new methods to assess PWV have been partially validated, the gold standard method of non-invasive assessment of PWV continues to be applanation tonometry [69], [75]–[77]. In general, pressure waveforms are gated with simultaneous electrocardiographs and are used to calculate the PWV between the two sites (carotid–femoral). Foot-to-foot PWV is calculated by determining the delay between the appearance of the pressure waveform foot in the carotid and femoral sites (Δt). The measurement of the tonometry transit distance is made using a measuring tape on the surface of the body connecting the carotid measuring site with the suprasternal notch and the suprasternal notch with the femoral measuring site, respectively. The aortic transit distance is estimated by subtracting two times the suprasternal notch–carotid distance from tonometry transit distance, to account for parallel transmission in the aorta and common carotid [78]. Finally, aortic PWV is estimated by dividing aortic transit distance by Δt, using a validated computerized system [75], [78]–[80].

Obesity and physical activity

One of the best and most economic method that can be used in the "fight" against obesity is certainly physical activity. Obesity is characterized by an unbalance in energy intake and expenditure ratio in favour of intake that produce an excess of fat storage. Consequently, to lose fat it is necessary to increase energy expenditure. Physical activity and physical exercises prolonged over long periods of time can generate energy deficit and induce weight loss [81]–[83]. However, just moving a little bit more is not enough. Physical exercise should be voluntary and organized to be efficient. It is widely demonstrated that voluntary exercise is the most important discretionary component of total daily energy expenditure and, as a result, it has the potential to affect energy balance [84]. Thus, it is necessary to rationally exercise over time to be efficient in weight loss.

Muscles consume energy synthetizing their "fuel" from fat and glycogen [85]. This fuel is the ATP that is produced by the oxidation of both fatty acids and glucose from the bloodstream and triglyceride and glycogen acquired from intramuscular stores [85]. The more ATP is requested to provide energy, the bigger is the amount of fat or glycogen involved in ATP generation, according to exercise intensity. When physical activity intensities are greater than approximately 60% maximal oxygen consumption (VO2max), blood glucose and muscle glycogen are the primary fuels oxidized to produce the necessary ATP. On the other hand, prolonged exercises at intensities lower that 60% VO2max promote fatty acid oxidation to produce energy [86].

According to this physiological process, it should be obvious that aerobic training at moderate intensity (lower that 60% VO2 max) may be the best way to lose weight and reduce obesity. Aerobic training at low-to moderate intensity is normally prescribed from physician because it is simple to practise, economic and provides several benefits in prevention and treatment of obesity and its comorbidity. Aerobic activity (also known as "cardio") is physical exercise of low to high intensity that depends primarily on the aerobic energy-generating process and involve all that light-to-moderate intensity activities that are sufficiently supported by aerobic metabolism and that can be performed for extended periods of time [87]. This activity is mostly supported by fatty acids oxidation and fat storage mobilization. Examples of aerobic activities are running and jogging, swimming, cycling and walking. First of all, aerobic exercise improve insulin sensitivity, reduce blood pressure and promotes weight loss when associated with a diet [88]–[90]. However, aerobic exercise seems to have small effects on Resting Metabolic Rate (RMR) and lean mass [91], [92]. Considering that RMR is the minimal amount of energy that a person needs to live a day in resting state, higher is RMR higher will be the daily energy consumption necessary to live. RMR can be strongly modified by resistance training because the goal of this training is to modify and increase the lean mass (muscles) [93] that is metabolically more active that fat mass. Consequently, the more metabolically active the mass is, the greater will be the daily expenditure to maintain the body alive.

Resistance training is an anaerobic activity intense enough to cause lactate formation and accumulation in the bloodstream. It is use when great amount of strength, speed and power is required. Additionally, because of its participation in strength and power, muscle mass growth is promoted. Muscle energy system involved in resistance training comes from stored ATP and from a limited supply of stored muscle glycogen, necessary to support intense activity that last from some seconds to up to two minutes [87]. A specific amount of recovery among sets is necessary to restore ATP and muscle glycogen, in order to allow to perform exercise another time. Examples of anaerobic activities are weightlifting and sprinting. Resistance training can improve insulin sensitivity as aerobic training does [94]. In addition, a great meta-analysis of De Sousa and colleagues [95] underlines as resistance training alone provides reduction in systolic blood pressure so it may be a good tool to manage systemic hypertension. Weight loss reduction is dispensed by increasing in lean mass and RMR. Moreover, resistance training affect the self-concept in young obese adolescents, leading them to continue and improve physical activity and to avoid desertion [96]. Finally, actual guidelines suggest utilizing resistance training in the management of obesity through physical activity.

A combined approach (aerobic and resistance training in the same session) is starting to be purposed but it is difficult to identify standardized combination of aerobic and resistance training. Actually, HIIT (High Intensity Interval Training) is becoming very popular thanks to its positive effect on physical fitness and fat mass reduction in a lower amount of time [97]

However, HIIT is not properly recommended for beginners because of the high intensities of exercises that require a good background in technical execution of specific movements and body motor control.

Aim of the study

The aim of this study is to identify changes in cardiovascular profile and body composition due to resistance or combined training in a population of obese adolescents with and without hypertension. In addition, our second goal is to identify which kind of training may be the most suitable in terms of adherence to the program, tolerance to exercise and persistence over time in a population of obese adolescents.

METHODS

Subjects

This study was approved by the local ethical committee (AOU CIttà della Salute, Turin, Italy). Before starting the experimental phase, subjects were informed about the aim of the study. They have voluntary accepted to participate and their parents have given them the permission to be involved by signing and informed consent. Thirty-eight obese and fifteen healthy adolescents aged between 14 and 17 years were enrolled for this study. The recruitment process has been conducted in Molinette Hospital (AOU CIttà della Salute, Turin, Italy) in cooperation with Pediatric Division of Regina Margherita Hospital (AOU CIttà della Salute, Turin, Italy) and the School of Exercise and Sport Science (Department of Medical Science) of the University of Turin. Each subject was checked in an authorized centre of sport medicine in order to obtain the medical permission to practice physical activity. Seven subjects have decided to retire themselves from the program after medical check-up, so the study started with the remaining thirty-one participants. In addition, fifteen healthy adolescents were measured at baseline and considered as reference group for measurements of body composition. The inclusion criteria for that in concern the obese sample were as follow: “teen-age” at the beginning of the study, recognized obesity (BMI >30), sedentary lifestyle (less than 60 minutes of physical activity per week), no special diet or involvement in dietary programs, absence of hypertension, or moderate hypertension but not yet pharmacologically treated and no history of any medical condition that would prevent participation in the exercise intervention. The only pharmacological treatment that we accepted was metformin in that patient who showed a beginning of insulin-resistance. People that were not “teen-age”, unable to practise physical activity and/or pharmacologically treated for hypertension or other heart diseases were excluded from this study. On the opposite, healthy subjects should be life active (at least 120 minutes of organized physical activity per week), have a BMI lower that 26 and not to be pharmacologically treated for any disease to be included in the reference group. Total body fat percentages (acquired with bioelectrical impedance) for obese and healthy adolescents were 37%-44% and 11%-26% respectively. The subjects in the experimental group performed at least 60% of the training sessions on the 6-months-long experimental period. The training schedules were performed from January to June 2018 with the first part of the group (15 subjects) and from January to June 2019 for the second part (16 subjects). Enrolment process and subjects’ allocation are represented in figure 1 in the CONSORT 2010 flow diagram [98].

CONSORT

TRANSPARENT REPORTING of TRIALS

CONSORT 2010 Flow Diagram

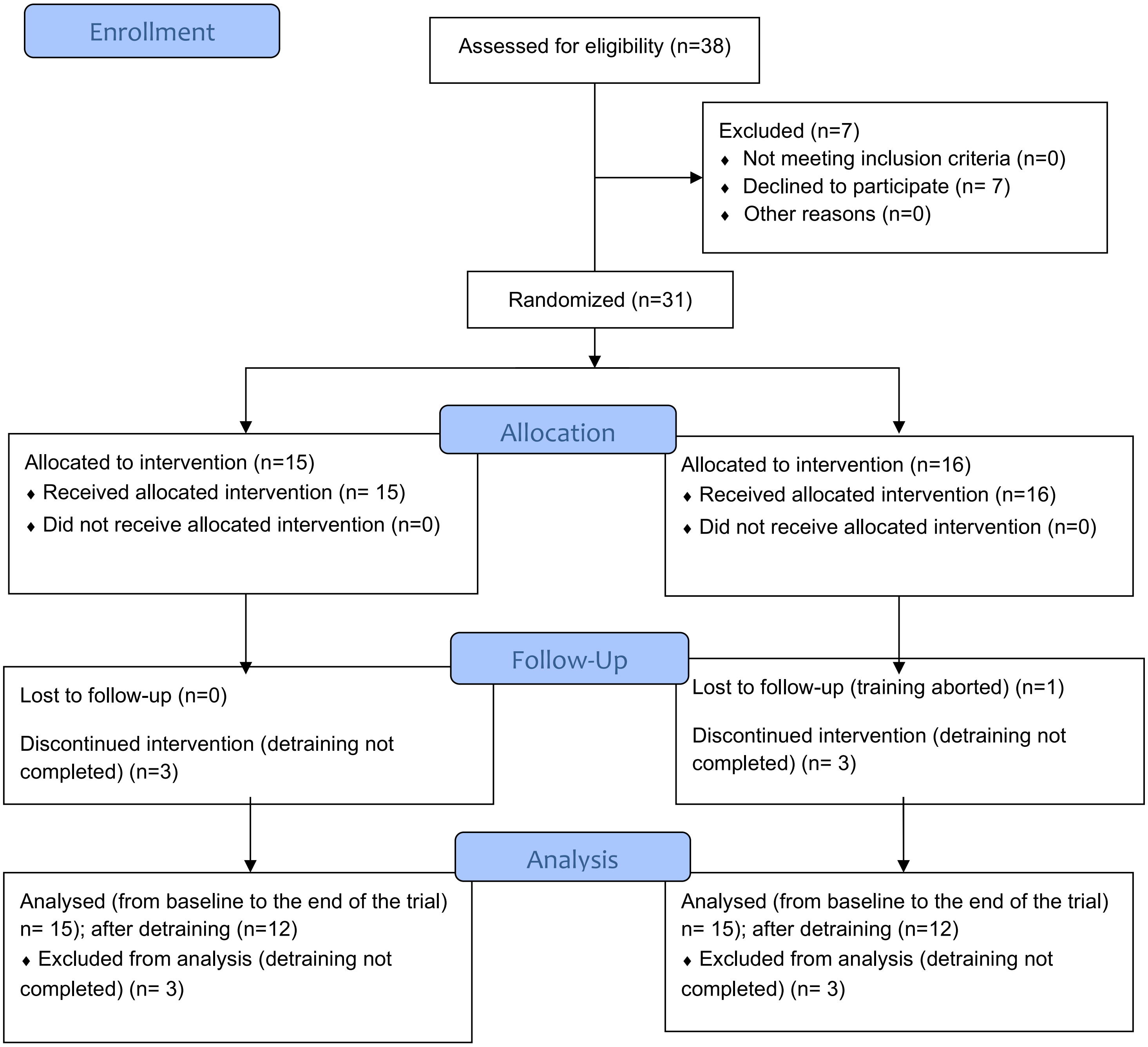

Figure 1. CONSORT 2010 flow diagram. The chart shows how subjects were enrolled and allocated in the study design.

Procedures

All obese participants were randomly assigned to one of the two training group. On the opposite, healthy adolescents performed only baseline measurement of body composition as reference group. Before starting, all subjects were checked up in hospital where they were evaluated on the following parameters: anthropometric measures (body weight, height, BMI, waist circumference, blood pressure, heart rate, breath rate) to assess clinical report; lipid profile, blood glucose and insulin values, homeostatic model evaluation – HOMA to analyse metabolic profile; 20 minutes ECG Holter monitoring, Ambulatory Blood Pressure Monitoring (ABPM) 24h with an actigraphic evaluation of physical activity and oximetry index, oxygen supply, transthoracic echo and wrist Pulse Wave Velocity (PWV) to measure the functionality of cardiovascular system. Furthermore, at baseline, eating habits and psychological profile were also defined through specific questionnaires. After that these measurements were completed, people were moved to the School of Exercise and Sport Science (Department of Medical Science) of the University of Turin to assess body composition and to receive their training program. On the opposite, healthy subjects moved directly to the School of Exercise and Sport Science to be evaluated on body composition. Evaluations were performed 3 times during the experimental period: at the beginning, at the end of the 6-months-long training program and after 3 months of detraining. Measurements were administrated at the same time of day for each subject. During training span all participants attended 2 non-consecutive training sessions (about 60 minutes long) a week for a total of 40 sessions during the entire period. Subjects could choose between these training days matching these purposes: Monday and Wednesday; Tuesday and Thursday or Wednesday and Friday. Exceptionally, we also accepted people who asked to train on Tuesday and Friday because of school duties. All the sessions were performed in the afternoon from 2 to 6 pm in a gym validated from the Faculty of Sport Science of the University of Turin and all the training sessions were supervised by certificated and sport graduated trainers. Adherence to training was acquired electronically by scanning the personal gym's season pass on the access gate in the period between January and June 2019. In the previous years, adherence was self-reported by signing on a properly signature sheet. Finally, all subjects were educated to follow a balanced diet and adherence to this nutritional behaviour was self-reported and registered during body composition analysis.

Data collections

Data were collected on three moments as follow: *First session (T0)* at the beginning of the study (January 2018 for the first part of the subjects involved and January 2019 for the second part), *Second session (T1)* at the end of the 6-months-long training period (June 2018 for the first part of the subjects involved and June 2019 for the second part) and *Third session (T2)* after 3 months of detraining (September 2018 for the first part of the subjects involved and September 2019 for the second part). Each session was completed on two separate days.

Blood Sampling, clinical report and metabolic profile

Blood sampling, urine analysis clinical report, metabolic and cardiovascular profile were evaluated in the first day blood sugar, insulin, serum creatinine, serum sodium, serum potassium, total cholesterol, hdl, triglycerides, uricemia, sodium excretion were traced from blood analysis. Anthropometric measures (body weight, height, BMI, waist circumference, blood pressure, heart rate, breath rate) were considered for clinical evaluation report. For that it concerns Metabolic profile, lipid profile, blood glucose and insulin values, homeostatic model evaluation – HOMA were assessed. HOMA index is based on a homeostatic mathematical model and it is used to calculate serum-glucose-related insulin resistance and fasting insulin concentration according to the following formula:

HOMA index = blood sugar (mmol/L) x insulin (mU/L) / 22.5

Cardiovascular Profile

Finally, Cardiovascular profile was evaluated through ECG Holter monitoring (20 minutes) to assess HRV, ABPM 24h with an actigraphic evaluation of physical activity and oximetry index, oxygen supply, transthoracic echo and wrist Pulse Wave Velocity (PWV).

ECG Holter monitoring was 20 minutes long and performed after some minutes of rest, in a quite a comfortable place with standardized condition of air temperature. ECG (including QT interval) was registered using Fukuda Denshi FM-180 device and software SCM-510 to process data. In addition, LH/FH ratio was reported to investigate sympatho-vagal responsiveness of cardiovascular system.

ABPM 24h was recorded using the Spacelabs 90207 (Spacelabs Inc. Redmond, Washington, USA). Monitoring started at 9 in the morning and finished the day after at same time. No physical or stressing activity were allowed during monitoring. Blood pressure was registered every 15 minutes over the course of 24 hours. Furthermore, blood pressure load was detected. It is defined as the percentage of abnormally elevated blood pressure readings during ABPM, considered when blood pressure exceeds the 95-percentile related for sex and height. Masked or isolated hypertension were also investigated to be excluded. Each participant should report all daily activities on a diary. Measures acquired during napping time were not considered in the analysis [99], [100].

Ultrasound scanner Philips iE33 (Bothell, Washington) was utilized for transthoracic echo evaluation. Left ventricular mass (LVM) was calculated from left ventricular internal diameter during telediastolic phase (LVIDd), from interventricular septum thickness (SWTd) and the inferior-lateral wall (ILW) according to the Devereux formula [101]:

$LVM = 0.8 (1.04 [(LVIDd + ILWd + SWTd)3 – LVIDd3] + 0.6$

Pulse wave velocity was “foot-to foot” calculated [102] using SphygmoCor SCOR-PVx System (Atcor Medical, Sydney, Australia).

Body Composition

On the second day of measurements, participants were moved to School of Exercise and Sport Science (Department of Medical Science) of the University of Turin to assess their body composition. People arrived in Adapted Training and Performance Laboratory of the School of Exercise and Sport Science from 8 to 9 am after a 10-h overnight fast and 8 h of sleep. Subjects removed their right sock and rested on a physiotherapy bed in a supine position for 15 min while bio-impedance machine was prepared. Lower limbs were 45^o open wide and upper limbs abducted of 30^o. A couple of electrodes were applied on the right foot and another couple on the right hand. The first electrode was attached between the second and the third finger both in the foot and hand, while the second one was applied to 5 cm. Body composition was acquired using a BIA-ACC Medical Device (Biotekna, Venice, Italy) able to analyse the following parameters: Body Mass Index (BMI), Total Body Water (TBW), , Free Fat Mass (FFM), Fat Mass (FM), Resting Metabolic Rate (RMR), Body Density, Bone, T-Score, Muscle, S-Score, Adipose Tissue (AT), Abdominal Adipose Tissue (AAT), Intra Muscolar Adipose Tissue (IMAT).

Training Program

Obese adolescents were randomly assigned to one of the two intervention groups: Resistance Training (RT) and Combined Training (CT). RT performed a counter-resistance training lifting weights while CT trained mixing both weights lifting and aerobic activities.

The 6-months-schedule was devised into three parts composed of two months each (table 2).

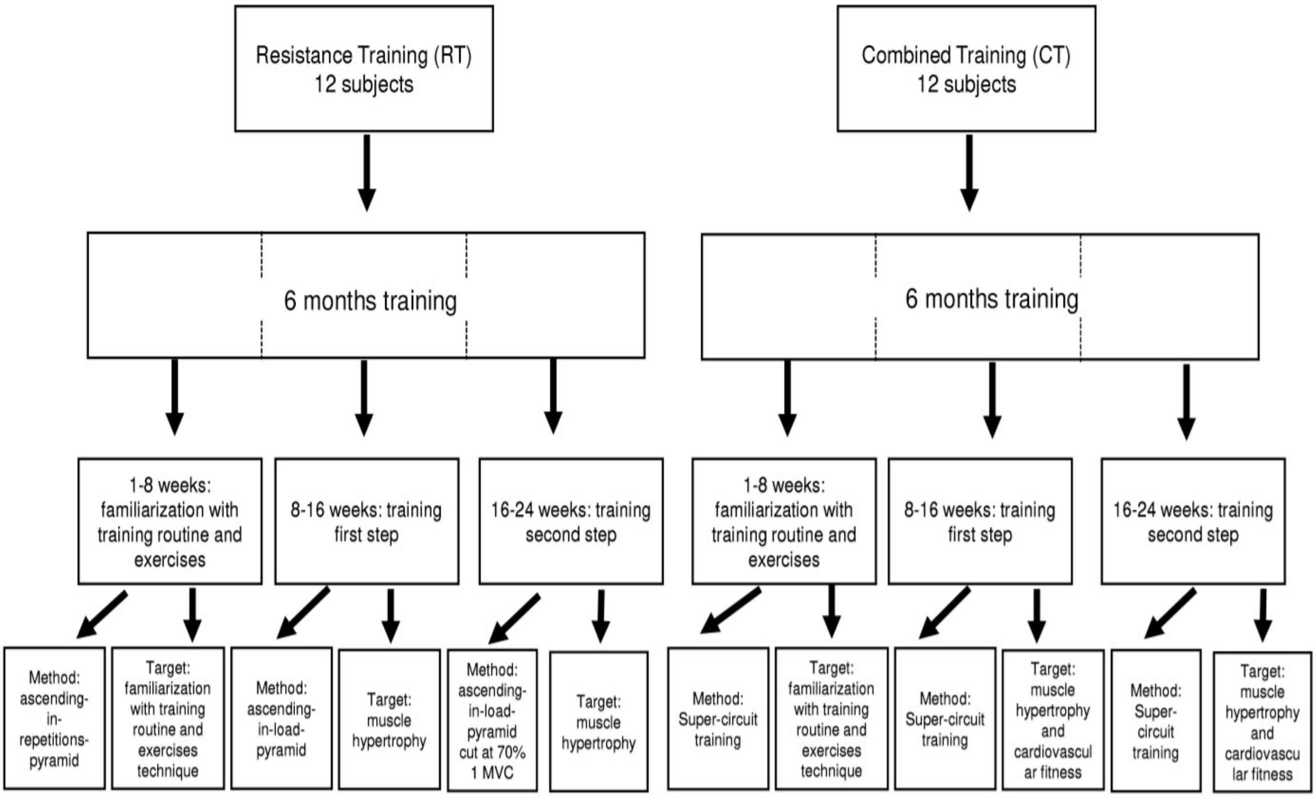

Table 2. Representation of training schedule for both resistance and combined training

Every session of each group was preceded by 15 minutes warm up (10 minutes cycling at low intensity maintaining 70-80 RPM and 5 minutes of active and dynamic stretching) and followed by a 5 minutes cool-down in which people performed some static stretching for lower and upper limbs. Work-out was different between the groups for that it concerns the main part of the schedule. RT lifted only weights in a total body routine. Eight exercises, one for each main muscle group were accomplished. Subjects started to train the core by performing crunches for rectus abdominis and hyperextensions for the lumbar muscles chain. Then, leg press for quadriceps, bench press for pectoralis major, lat machine for latissimus dorsi, shoulder press for deltoideus and, to conclude, biceps curl for biceps brachii and French press for triceps brachii. The *first period* has been intended as familiarisation and technical learning. People performed 3 sets using an ascending-in-repetitions-pyramid scheme. The first set was accomplished using 12 repetitions, the second with 15 and the third with 20. Every set was completed using an overweight of 45-

55% (low intensity) of their estimated 1 MVC (Maximal Voluntary Contraction). In the second *period* intensity increase up to 60% (low-to-moderate) of their estimated 1 MVC and the previous pyramid was reversed (20-15-12) Now the pyramid scheme is ascending in load and descending in repetitions. Finally, in the *third period*, intensity increased again up to 70% of estimated 1 MVC, pyramid was cut at the second increment off (1x12-10-10) in order not to exceed intensity limit of 70% of 1 MVC. Resting time among sets was standardised at 1 minutes and 30 second and was applied for the entire training period. In period two and three, 1 MVC was predicted using Brzycki formula [103]. Conversely, in period one load to lift was estimated according to subjects' sensations recorded using a VAS scale. Resistance training schedules are reported in the following table (Table 3):

RESISTANCE TRAINING SCHEDULE

WEEKS	EXERCISE	SET AND REPS	REST	INTENSITY	FREQUENCY	TARGET
1-8	Cycling on a cyclette	1 x 10min	/	60% MHR	2 times a week	warm up
	Crunches	1 x 12-15-20	1 min 30 sec	45-50% 1 MVC	2 times a week	rectus abdominis
	perextention (lower back machine	1 x 12-15-20	1 min 30 sec	45-50% 1 MVC	2 times a week	lumbar muscles strain
	Leg Press	1 x 12-15-20	1 min 30 sec	45-50% 1 MVC	2 times a week	quadriceps
	Bench Press	1 x 12-15-20	1 min 30 sec	45-50% 1 MVC	2 times a week	pectoralis major
	Lat Machine	1 x 12-15-20	1 min 30 sec	45-50% 1 MVC	2 times a week	latissiums dorsi
	Shoulder Press	1 x 12-15-20	1 min 30 sec	45-50% 1 MVC	2 times a week	deltoideus
	Biceps Curl	1 x 12-15-20	1 min 30 sec	45-50% 1 MVC	2 times a week	biceps brachii
	Push Down	1 x 12-15-20	1 min 30 sec	45-50% 1 MVC	2 times a week	triceps brachii
	Static Stretching	during rest pauses	/	/	2 times a week	whole body
	Cycling on a cyclette	1 x 10min	/	60% MHR	2 times a week	cool down
8-16	Cycling on a cyclette	1 x 10min	/	60% MHR	2 times a week	warm up
	Crunches	1 x 20-15-12	1 min 30 sec	55-65% 1 MVC	2 times a week	rectus abdominis
	perextention (lower back machine	1 x 20-15-12	1 min 30 sec	55-65% 1 MVC	2 times a week	lumbar muscles strain
	Leg Press	1 x 20-15-12	1 min 30 sec	55-65% 1 MVC	2 times a week	quadriceps
	Bench Press	1 x 20-15-12	1 min 30 sec	55-65% 1 MVC	2 times a week	pectoralis major
	Lat Machine	1 x 20-15-12	1 min 30 sec	55-65% 1 MVC	2 times a week	latissiums dorsi
	Shoulder Press	1 x 20-15-12	1 min 30 sec	55-65% 1 MVC	2 times a week	deltoideus
	Biceps Curl	1 x 20-15-12	1 min 30 sec	55-65% 1 MVC	2 times a week	biceps brachii
	Push Down	1 x 20-15-12	1 min 30 sec	55-65% 1 MVC	2 times a week	triceps brachii
	Static Stretching	during rest pauses	/	/	2 times a week	whole body
	Cycling on a cyclette	1 x 10min	/	60% MHR	2 times a week	cool down
16-24	Cycling on a cyclette	1 x 10min	/	60% MHR	2 times a week	warm up
	Crunches	1 x 12-10-10	1 min 30 sec	65-70% 1 MVC	2 times a week	rectus abdominis
	perextention (lower back machine	1 x 12-10-10	1 min 30 sec	65-70% 1 MVC	2 times a week	lumbar muscles strain
	Leg Press	1 x 12-10-10	1 min 30 sec	65-70% 1 MVC	2 times a week	quadriceps
	Bench Press	1 x 12-10-10	1 min 30 sec	65-70% 1 MVC	2 times a week	pectoralis major
	Lat Machine	1 x 12-10-10	1 min 30 sec	65-70% 1 MVC	2 times a week	latissiums dorsi
	Shoulder Press	1 x 12-10-10	1 min 30 sec	65-70% 1 MVC	2 times a week	deltoideus
	Biceps Curl	1 x 12-10-10	1 min 30 sec	65-70% 1 MVC	2 times a week	biceps brachii
	Push Down	1 x 12-10-10	1 min 30 sec	65-70% 1 MVC	2 times a week	triceps brachii
	Static Stretching	during rest pauses	/	/	2 times a week	whole body
	Cycling on a cyclette	1 x 10min	/	60% MHR	2 times a week	cool down

Table 3. Resistance training schedule

On the other hand, CT accomplished both weightlifting and aerobic exercises in the same session. This group worked-out with a “super-circuit design”, where a weightlifting exercise is followed by aerobic activity maintained for a certain amount of time. Weightlifting procedures were the same as RS about exercises routine, resting time among sets and prediction of 1 MVC. Differently, CT accomplished only two set each period. Repetitions grew gradually: 8-10 (eight in the first set and ten in the second) in the first period, 12-15 in the second and 15-20 in the third. Intensity grew slightly from 45% up to 60% of 1 MVC. Pyramid scheme is respected only in repetitions, while load remain the same in each period. Aerobic activity was practised on cyclette or elliptical machine. In each period, participants practised 30-35 minutes of weightlifting and 30 minutes of aerobic activity organizes as follow: one counter-resistance exercise followed by 5 minutes of aerobic activity at moderate intensity in the *first period*. Two consecutive counter-resistance exercises followed by 10 minutes of aerobic activity at moderate intensity in the *second period*. Finally, in the *third period* three consecutive counter-resistance exercises were accomplished before practising 15 minutes of aerobic activity. Training design for this group is represented in the following table (Table 4):

COMBINED TRAINING SCHEDULE						
WEEKS	EXERCISE	SET AND REPS	REST	INTENSITY	FREQUENCY	TARGET
1-8	Crunches	1 x 8-10	1 min 30 sec	40-45% 1 MVC	2 times a week	rectus abdominis
	Cycling on a cyclette	1 x 5 min	/	65% MHR	2 times a week	cardiovascular fitness
	perextention (lower back machine	1 x 8-10	1 min 30 sec	40-45% 1 MVC	2 times a week	lumbar muscles strain
	Cycling on a cyclette	1 x 5 min	/	65% MHR	2 times a week	cardiovascular fitness
	Leg Press	1 x 8-10	1 min 30 sec	40-45% 1 MVC	2 times a week	quadriceps
	Cycling on a cyclette	1 x 5 min	/	65% MHR	2 times a week	cardiovascular fitness
	Bench Press	1x 8-10	1 min 30 sec	40-45% 1 MVC	2 times a week	pectoralis major
	Cycling on a cyclette	1 x 5 min	/	65% MHR	2 times a week	cardiovascular fitness
	Lat machine	1x 8-10	1 min 30 sec	40-45% 1 MVC	2 times a week	latissiums dorsi
	Cycling on a cyclette	1 x 5 min	/	65% MHR	2 times a week	cardiovascular fitness
	Shoulder Press	1x 8-10	1 min 30 sec	40-45% 1 MVC	2 times a week	deltoideus
	Cycling on a cyclette	1 x 5 min	/	65% MHR	2 times a week	cardiovascular fitness
	Biceps Curl	1 x 8-10	1 min 30 sec	40-45% 1 MVC	2 times a week	biceps brachii
	Push Down	1 x 8-10	1 min 30 sec	40-45% 1 MVC	2 times a week	triceps brachii
	Static Stretching	during rest pauses	/	/	2 times a week	whole body
	whole body stretching	5 minutes	/	/	2 times a week	cool down
8-16	Crunches	1 x 12-15	1 min 30 sec	50-55% 1 MVC	2 times a week	rectus abdominis
	perextention (lower back machine	1 x 12-15	1 min 30 sec	50-55% 1 MVC	2 times a week	lumbar muscles strain
	Cycling on a cyclette	1 x 10 min	/	70-75% MHR	2 times a week	cardiovascular fitness
	Leg Press	1 x 12-15	1 min 30 sec	50-55% 1 MVC	2 times a week	quadriceps
	Bench Press	1 x 12-15	1 min 30 sec	50-55% 1 MVC	2 times a week	pectoralis major
	Cycling on a cyclette	1 x 10 min	/	70-75% MHR	2 times a week	cardiovascular fitness
	Lat machine	1 x 12-15	1 min 30 sec	50-55% 1 MVC	2 times a week	latissiums dorsi
	Shoulder Press	1 x 12-15	1 min 30 sec	50-55% 1 MVC	2 times a week	deltoideus
	Cycling on a cyclette	1 x 10 min	/	70-75% MHR	2 times a week	cardiovascular fitness
	Biceps Curl	1 x 12-15	1 min 30 sec	50-55% 1 MVC	2 times a week	biceps brachii
	Push Down	1 x 12-15	1 min 30 sec	50-55% 1 MVC	2 times a week	triceps brachii
	Cycling on a cyclette	1 x 5 min	/	60% MHR	2 times a week	cool down
	Static Stretching	during rest pauses	/	/	2 times a week	whole body
16-24	Crunches	1 x 12-15	1 min 30 sec	60% 1 MVC	2 times a week	rectus abdominis
	perextention (lower back machine	1 x 12-15	1 min 30 sec	60% 1 MVC	2 times a week	lumbar muscles strain
	Leg Press	1 x 12-15	1 min 30 sec	60% 1 MVC	2 times a week	quadriceps
	Cycling on a cyclette	1x 15 min	/	75-80% MHR	2 times a week	cardiovascular fitness
	Bench Press	1 x 12-15	1 min 30 sec	60% 1 MVC	2 times a week	pectoralis major
	Lat machine	1 x 12-15	1 min 30 sec	60% 1 MVC	2 times a week	latissiums dorsi
	Shoulder Press	1 x 12-15	1 min 30 sec	60% 1 MVC	2 times a week	deltoideus
	Cycling on a cyclette	1x 15 min	/	75-80% MHR	2 times a week	cardiovascular fitness
	Biceps Curl	1 x 12-15	1 min 30 sec	60% 1 MVC	2 times a week	biceps brachii
	Push Down	1 x 12-15	1 min 30 sec	60% 1 MVC	2 times a week	triceps brachii
	Cycling on a cyclette	1 x 5 min	/	60% MHR	2 times a week	cool down
	Static Stretching	during rest pauses	/		2 times a week	whole body

Table 4. Combined training schedule

Statistical analysis

Data were analysed using IBM SPSS Statistics 22.0 (for Windows) and GraphPad Prism 5 (for Windows). The Kolmogorov-Smirnov test was used to examine the normality of the data. Mann-Whitney tests for unpaired data were used to determinate the differences at baseline between groups.

Data are presented as the mean ± SD when normal, or as the median (25°-75° percentile) when not normal. Statistical significance was set at $P < 0.05$

Wilcoxon signed-rank test was used to determinate the effects of the two different types of physical activity over time. Spearman's correlation was used to identify possible associations between variables. Finally, Friedman test was used to determinate the effects of three months of detraining on body composition variables only.

RESULTS

Adherence to training and diet

Adherence to training was calculated electronically on a total amount of 40 training sessions, while adherence to dietary advices was self-reported on a scale of 10. Averaged adherence to training was 57% (23 training sessions on 40) and self-reported adherence to dietary advices was 3 on 10.

Anthropometrics and clinical features

Thirty-one obese adolescents were involved in a 6-months-training program. The 62,5% of them were obese from at least 5 years, while severe obesity (BMI ≥ 35) was identified in the 37,5% of the sample. Nobody was previously involved in any sport or physical activity. The mean age of the sample was 15.5 ± 1.55 years (range 13 to 18 years), height 164 ± 6.50 and prevalence of male was 43.8% equally distributed in both groups. The sample mean BMI was 33.3 ± 5.1 kg/m^2 and the prevalence of clinic hypertension was 18.8%. Cardiac autonomic function was altered in most of the subjects (SDNN 66.8 ± 33.3ms, LF/HF 1.71 ± 0.77). One participant decided to abort the program and was excluded from the study. The remaining 30 subjects completed the 6-months-program randomly associated to one of the two training group. No differences in mean weight (CT: 87.1 ± 16.8 vs. RT: 87 ± 17.7 Kg, p=0.9), BMI (CT: 34.8 ± 7.2 vs. RT: 31.3 ± 3.1, p=0.4) and body composition parameters (table 5) were observed between groups at baseline. A significant decrease in office diastolic blood pressure (DBP) (75 ± 7.2 vs. 68 ± 6.9 mmHg, p=0.004) and heart rate (HR) (84 ± 17.1 vs. 74 ± 10.4 bpm, p=0.04) was identified in both group after 6 months of training but no differences were noticed when groups were compared. In addition, an improvement of HRV parameters in both groups and a decrease in hypertension prevalence was identified in both groups at the end of the training protocol.

RESISTANCE TRAINING VS COMBINED TRAINING AT BASELINE

PARAMETER	RESISTANCE TRAINING (16)	COMBINED TRAINING (15)	p value
Weight (KG)	87.0 ± 17.7	87.1 ± 16.8	=0.900
BMI (Kg/m^2)	31.84 ± 4.172	31.89 ± 5.278	=0.566
%TBW (total body water)	39.76 ± 4.320	39.60 ± 3.996	=0.968
%FFM (free fat mas)	59.31 ± 4.6827	59.27 ± 5.230	=0.921
%FM (fat mas)	40.69 ± 4.827	40.73 ± 5.230	=0.921
BMR (basal metabolic rate)(kcal/die)	1474 ± 129.8	1456 ± 123.6	=0.678
Body Density (g/cm^3)	1.005 ± 0.008	1.005 ± 0.009	=1.000
Bone (kg)	3.96 ± 0.699	3.82 ± 0.683	=0.570
T-Score	-0.22 ± 0.640	-0.10± 0.694	=0.677
Muscle (kg)	20.29 ± 4.550	19.35 ± 4.429	=0.527
S-score	1.11 ± 0.984	1.43 ± 1.087	=0.451
AAT (addominal adipose tissue) (cm^2)	613.3 ± 211.0	594.0 ± 239.2	=0.593
% IMAT (Intra Muscolar Adipose Tissue)	2.269 ± 0.340	2.207 ± 0.385	=0.591
AT (Adipose Tisssue) (Kg)	45.20 ± 13.96	44.76 ± 15.44	=0.693

Table 5. Groups at baseline. Body composition parameters were acquired with BIA-ACC Medical Device (Biotekna s.r.l., Italy). No differences were detected between groups at baseline.

Metabolic profile

Participants' metabolic profile is presented in table 6. It is important to notice high values of HOMA-index (3.9 ± 2,1 mcU/ml) even if blood sugar levels were in normal range (blood sugar 82.1± 7,2 mg/dl). Prevalence of insulin-resistance was identified in 62,3% of the sample considering as cut off the reference HOMA-index set at 3,54 to determinate insulin-resistance. For this reason, further analysis was necessary to verify if this condition affected outcomes compared to non-insulin-resistant people (table 7). No differences were registered at baseline between groups and between insulin and non-insulin-resistant).

A significant decrease in blood triglycerides (p=0,037) was found after 24 weeks of training in the whole sample. In addition, a trend to significant increase of HDL values (p=0,067, table 8) was found in the whole sample with no differences within groups. Non significance difference was found in all other variables.

INSULIN-RESISTANCE VS NON-INSULIN-RESISTANCE

PARAMETER	INSULIN-RESISTANCE	NON-INSULIN-RESISTANCE	p value
Weight (kg)	90 ± 19.9	83 ± 9.9	=0.471
Height (cm)	161 ± 7.5	162 ± 7.8	=0.739
BMI (kg/m2)	34.4 ± 5.9	31.5 ± 3.0	=0.291
BMI z-score	2.2 ± 0.3	1.9 ± 0.4	=0.067
Waist circumference (cm)	100 ± 15.6	94 ± 10.7	=0.464
Clinic SBP (mmHg)*	124 ± 8.8	118 ± 6.9	**=0.028**
Clinic DPB (mmHg)	76 ± 7.0	74 ± 8.0	=0.638
Clinic Hearth rate (bpm)	88 ± 20.7	78 ± 3.8	=0.243
Total cholesterol (mg/dl) *	171 ±12.4	165 ± 22.2	**=0.021**
HDL (mg/dl)	45 ± 4.9	54 ± 16.9	=0.240
TG (mg/dl) *	116 ± 39.4	69 ± 31.5	**=0.025**
LDL (mg/dl)	103 ±17.9	97 ± 9.7	=0.402
SBP 24 hours (mmHg)	119 ± 6.7	116 ± 10.3	=0.514
DBP 24 hours (mmHg)	66 ± 4.6	65 ± 4.5	=0.506
Heart rate 24 hours (bpm)	83 ± 10.6	75 ± 7.8	=0.149
SBP daily (mmHg)	123 ± 7.4	115 ± 7.9	=0.072
Daytime DBP (mmHg)	70 ± 5.2	66 ± 4.3	=0.113
Daytime Heart rate (bpm)	86 ± 10.9	78 ± 8.5	=0.166
Night SBP (mmHg)	110 ± 8.4	106 ± 11.9	=0.517
Night DPB (mmHg)	58 ± 5.4	56 ± 2.6	=0.330
Night Heart rate (bpm)	77 ± 12.6	71 ± 6.1	=0.325
SDNN (ms)	63.5 ± 33.5	72.3 ± 35.4	=0.626
SDANN (ms)*	13.9 ± 14.1	20.8 ± 12.8	=0.050
RMSSD (ms)	48.1 ± 37.2	60.7 ± 42.9	=0.546
QTc (ms)	346.8 ± 23.4	346.8 ± 23.4	=0.996
LF (NU)	0.37 ± 0.1	0.29 ± 0.1	=0.230
HF (NU)	0.21 ± 0.1	0.26 ± 0.1	=0.493
LF/HF *	2.0 ± 0.8	1.3 ± 0.2	**=0.029**
LVMI (g/m$^{2.7}$)	31.7 ± 6.8	29.2 ± 8.6	=0.551
PWV m/s	5.7 ± 0.7	5.5 ± 0.5	=0.448
Central SBP (mmHg)*	108 ± 12.4	97 ± 4.1	**=0.023**
Central DPB (mmHg)	74 ± 9.5	66 ± 6.7	=0.119
TBW (%)	40.3 ± 4.8	40.0 ± 1.9	=0.857
FFM (%)	57.9 ± 5.9	60.2 ± 3.4	=0.438
FM (%)	42.1 ± 5.8	39.8 ± 3.4	=0.438
BMR (Kcal/die)	1476 ± 132.6	1454 ± 99.2	=0.751
AT (Kg)	48.8 ± 18.6	41.8 ± 8.2	=0.447
ATT (cm2)	669.4 ± 283.4	548.5 ± 130.0	=0.390
IMAT (Kg)	2.2 ± 0.9	1.8 ± 0.4	=0.317

Table 6. Differences between insulin and non-insulin resistance at baseline. Body composition parameters were acquired with BIA-ACC Medical Device (Biotekna s.r.l., Italy).

METABOLIC PROFILE OF THE WHOLE SAMPLE AT BASELINE

PARAMETER	RESISTANCE TRAINING (16)	COMBINED TRAINING (15)	p value
Blood sugar (mg/dl)	80.77±6.77	83.5 ± 7.68	=0.348
Insulin (mcUI/dl)	17.46 ± 10.25	17.43 ± 9.5	=0.994
Creatin (mg/dl)	0.75 ± 0.16	0.70 ± 0.14	=0.43
Sodium (mmol/l)	140.2 ± 2.3	140.4 ± 1.20	=0.843
Potassium (mmol/l)	4.64 ± 0.25	4.58 ± 0.23	=0.584
Total Chol. (mg/dl)	158.0 ± 12.22	168.73 ± 19.84	=0.229
HDL (mg/dl)	52.16 ± 16.65	50.36 ± 14.80	=0.781
TG (mg/dl)	86.75 ± 41.25	96.18 ± 37.27	=0.571
LDL (mg/dl)	93.82 ± 12.73	99.09 ± 17.37	=0.455
Uricemia (mg/dl)	5,5 ± 0. 877	5.87 ± 0.98	=0.366
HOMA-i (mcU/ml)	3.70 ± 1.20	3.83 ± 2.33	=0.855

Table 7. Metabolic profile of the whole sample at baseline. No differences were detected between resistance and combined training group at baseline.

METABOLIC PROFILE OF THE WHOLE SAMPLE AFTER 24 WEEKS OF TRAINING

PARAMETER	BASELINE	AFTER 24 WEEKS OF TRAINING	p value
Blood sugar (mg/dl)	82.08 ± 7.22	78.36 ± 5.00	=0.075
Insulin (mcUI/dl)	17.46 ± 10.25	17.43 ± 9.5	=0.241
Total Chol. (mg/dl)	158.0 ± 12.22	168.73 ± 19.84	=0.423
HDL (mg/dl)	52.16 ± 16.65	50.36 ± 14.80	=0.067
TG (mg/dl) *	91.26 ± 38.85	76.28 ± 27.06	**=0.037**
LDL (mg/dl)	93.82 ± 12.73	99.09 ± 17.37	=0,297
HOMA-i (mcU/ml)	3.70 ± 1.20	3.83 ± 2.33	=0,262

Table 8. Metabolic profile of the whole sample after 24 weeks of training. No differences were detected between resistance and combined training group after the training schedule.

Cardiovascular profile

Cardiovascular profile outcomes at baseline are shown in table 9. No significant differences are detected at baseline between groups and all the variables are in reference range for age and sex [104], [105]. No differences were detected in all variables in both groups after 24 weeks of training. (table 9a and 9b).

CARDIOVASCULAR PROFILE OF THE WHOLE SAMPLE AT BASELINE

PARAMETER	RESISTANCE TRAINING (16)	COMBINED TRAINING (15)	p value
SDNN (ms)	69.85 ± 35.22	56.87 ± 29.92	=0.318
SDANN (ms)	22.56 ± 20.16	17.43 ± 9.5	=0.206
RMSSD (ms)	51.13 ± 36.02	44.33 ± 21.79	=0.243
QTc (ms)	356.43 ± 22.78	342.37 ± 1.295	=0.114
LF (NU)	1730.71 ± 1570.39	1117.04 ± 1002.66	=0.303
HF (NU)	17433.21 ± 1737.24	726.83 ± 677.27	=0.216
LF/HF	2.10 ± 1.37	1.77 ± 1.72	=0.969
PWV m/s	5.48 ± 0.62	5.25 ± 0.64	=0.279
Central SBP (mmHg)	103.2± 11.15	102.38 ± 8.29	=0.719
Central DBP (mmHg)	68.35 ± 10.25	74.25 ± 6.97	=0.096

Table 9. Cardiovascular profile of the whole sample at baseline. No differences were detected between resistance and combined training group at baseline.

CARDIOVASCULAR CHANGES AFTER 24 WEEKS OF RESISTANCE TRAINING

PARAMETER	BASELINE (16)	AFTER 24 WEEKS OF TRAINING (16)	p value
SDNN (ms)	69.85 ± 35.22	79.03 ± 50.48	=0.811
SDANN (ms)	22.56 ± 20.16	19.32 ± 22.86	=0.507
RMSSD (ms)	51.13 ± 36.02	59.44 ± 59.50	=0.173
QTc (ms)	356.43 ± 22.78	370.36 ± 32.36	=0.224
LF (NU)	1730.71 ± 1570.39	1908.33 ± 2447.8	=0.470
HF (NU)	17433.21 ± 1737.24	2284.17 ± 4440.24	=0.569
LF/HF	2.10 ± 1.37	1.82 ± 1.37	=0.258
LVMI (g/m$^{2.7}$)	27.55 ± 6.33	33.67 ± 7.13	=0.102
PWV m/s	5.48 ± 0.62	5.48 ± 0.85	=0.987
Central SBP (mmHg)	100.6 ± 11.12	106.00 ± 7.76	=0.104
Central DBP (mmHg)	68.35 ± 10.25	68.67 ± 8.25	=0.723

Table 9a. Cardiovascular profile of resistance training group after 24 weeks of training. No differences were detected between baseline and after the training schedule.

CARDIOVASCULAR CHANGES AFTER 24 WEEKS OF COMBINED TRAINING

PARAMETER	BASELINE (16)	AFTER 24 WEEKS OF TRAINING (15)	p value
SDNN (ms)	56.87 ± 29.92	62.37 ± 27.32	=0.470
SDANN (ms)	17.43 ± 9.5	17.38 ± 11.45	=0.439
RMSSD (ms)	44.33 ± 21.79	51.09 ± 35.64	=0.135
QTc (ms)	342.37 ± 1.295	358.41 ± 26.71	=0.070
LF (NU)	1117.04 ± 1002.66	1420.83 ± 1117.59	=0.205
HF (NU)	726.83 ± 677.27	978.33 ± 1168.44	=0.237
LF/HF	1.77 ± 10.72	2.35 ± 1.48	=0.210
PWV m/s	5.48 ± 0.85	5.06 ± 0.61	=0.085
Central SBP (mmHg)	104.56 ± 10.70	99.44 ± 7.60	=0.070
Central DBP (mmHg)	74025 ± 6.97	69.18 ± 7.49	=0.089

Table 9b. Cardiovascular profile of combined training group after 24 weeks of training. No differences were detected between baseline and after the training schedule.

Body composition

Body composition parameters are shown in Table 10a (RT) and 10b (CT), while reference group is represented in Table 10 compared with the whole sample. As reference group, we enrolled fifteen healthy active adolescents (height 17 ± 7.8 cm, weight 64 ± 6.5 cm, BMI 21.0 ± 2.9 Kg/m^2). At baseline, all parameters were significantly different from the whole sample ($p < 0,001$) except RMR. MUSCLE AND BONE that were not significance ($p = 0,725$, 0,282 and 0,646 respectively; Table 10). However, the whole sample showed better scores in T-Score ($p < 0,05$) and S-Score ($p < 0,001$).

Comparing the two training groups, results show stronger significative reduction of Fat Mass in RT (FM, RT $p < 0,01$ vs CT $p < 0,05$). On the opposite, Adipose Tissue and Abdominal Adipose Tissue depletion was greater in CT (AT and AAT, RT $p < 0,05$ vs CT $p < 0,01$). Intra Muscolar Adipose Tissue showed stronger differences in RT (IMAT, RT $p < 0,01$ vs CT $p < 0,05$) after 6-months-training program.

Moreover, RT revealed stronger increments in Total Body Water (TBW, RT $p<0,001$ vs CT $p< 0,01$) and RMR (RT $p< 0,01$ vs CT $p< 0,05$) while Free Fat Mass and Body Density increased in both groups (FFM $p< 0,05$, Body Density $p<0,01$ for both groups).

Finally, Bone Mass ($p<0,01$), T-score ($p<0,01$), Muscle Mass ($p<0,05$) and S-Score ($p<0,01$) were increased just in RT while BMI were significantly reduced only in CT ($p< .05$). In addition, we analysed the effects of twelve weeks of detraining on body composition using the Friedman Test and it was noticed that, FM, AAT and AT were significantly increased after 12 weeks of detraining (Friedman test $p< 0,001$; Dunn's post hoc $p< 0,01$), while TBW, FFM and Body density were significantly decreased (Friedman test $p< 0,001$; Dunn's post hoc $p< 0,01$) (Table 11)

INTERVENTION VS REFERENCE AT BASELINE

PARAMETER	INTERVENTION (30)	REFERENCE (15)	p value
BMI (Kg/m^2)	33 ± 5.106	21.6 ± 3.2	**<0,001**
%TBW (total body water)	40 ± 4.202	56.5 ± 5.9	**<0,001**
%FFM (free fat mas)	60 ± 4.667	80.1 ± 8.3	**<0,001**
%FM (fat mas)	40 ± 4.667	19.9 ± 8.3	**<0,001**
BMR (basal metabolic rate)(kcal/die)	1458 ± 115.521	1466 ± 122.5	=0.725
Body Density (g/cm^3)	1.006 ± 0.009	1.049 ± 0.018	**<0,001**
Bone (kg)	3.91± 0.679	4.0 ± 0.539	=0.282
T-Score	-0.3 ± 0.675	-0.7 ± 0.553	**<0,05**
Muscle (kg)	20.07 ± 4.426	19.7 ± 3.371	=0.646
S-score	1.30 ± 1.188	-0.5 ± 0.668	**<0,001**
AAT (addominal adipose tissue) (cm^2)	631.13 ± 234.260	205.9 ± 147.6	**<0,001**
% IMAT (Intra Muscolar Adipose Tissue)	2.3 ± 0.318	205.9 ± 147.6	**<0,001**
AT (Adipose Tisssue) (Kg)	44 ± 12.775	17.1 ± 9.7	**<0,001**

Table 10. Intervention vs Reference group at baseline. Body composition parameters were acquired with BIA-ACC Medical Device (Biotekna s.r.l., Italy). Significance was set at $p< 0.05$. Reference group shows generally better scores, apart from T-Score and S-Score, where intervention is significantly better. RMR, BONE and MUSCLE mass are no different between reference and intervention group.

BODY COMPOSTION CHANGES AFTER 24 WEEKS OF RESISTANCE TRAINING

PARAMETER	BASELINE (15)	AFTER 24 WEEKS OF RESISTANCE TRAINING (15)	p value
BMI (Kg/m^2)	31.84 ± 4.172	31.28± 3.896	=0.255
%TBW (total body water)	39.76 ± 4.320	42.43 ±4.700	**<0.001**
%FFM (free fat mas)	59.31 ± 4.6827	61.19 ± 4.875	**<0.01**
%FM (fat mas)	40.69 ± 4.827	38.81 ± 4.875	**<0.01**
BMR (basal metabolic rate)(kcal/die)	1474 ± 129.8	1508 ± 120.8	**<0.01**
Body Density (g/cm^3)	1.005 ± 0.008	1.010 ± 0.009	**<0.01**
Bone (kg)	3.96 ± 0.699	4.17 ± 0.713	**<0.01**
T-Score	-0.22 ± 0.640	0.6 ± 0594	**<0.01**
Muscle (kg)	20.29 ± 4.550	21.08 ± 3.746	**<0.05**
S-score	1.11 ± 0.984	1.49 ± 1.002	**<0.01**
AAT (addominal adipose tissue) (cm^2)	613.3 ± 211.0	575.6 ± 195.5	**<0.05**
% IMAT (Intra Muscolar Adipose Tissue)	2.269 ± 0.340	2.150 ± 0.332	**<0.01**
AT (Adipose Tisssue) (Kg)	45.20 ± 13.96	42.66 ± 12.95	**<0.05**

Table 10a. Body composition changes after 24 weeks of resistance training. Parameters were acquired with BIA-ACC Medical Device (Biotekna s.r.l., Italy). Significance was set at $p< 0.05$. Except for BMI, all parameters are significantly changed after 24 weeks of resistance training.

BODY COMPOSTION CHANGES AFTER 24 WEEKS OF COMBINED TRAINING

PARAMETER	BASELINE (16)	AFTER 24 WEEKS OF COMBINED TRAINING (15)	p value
BMI (Kg/m^2)	31.89 ± 5.278	31.30± 5.118	**<0.05**
%TBW (total body water)	39.60 ± 3.996	41.50 ±4.146	**<0.01**
%FFM (free fat mas)	59.27 ± 5.230	61.14 ± 5.885	**<0.01**
%FM (fat mas)	40.73 ± 5.230	40.14 ± 8.887	**<0.05**
BMR (basal metabolic rate)(kcal/die)	1456 ± 123.6	1474 ± 117.8	**<0.05**
Body Density (g/cm^3)	1.005 ± 0.009	1.09 ± 0.012	**<0.01**
Bone (kg)	3.82 ± 0.683	3.95 ± 0.584	=0.096
T-Score	-0.10± 0.694	0.050 ± 0645	=0.083
Muscle (kg)	19.35 ± 4.429	19.84± 4.156	=0.362
S-score	1.43 ± 1.087	1.53 ± 1.523	=0.914
AAT (addominal adipose tissue) (cm^2)	594.0 ± 239.2	563.8 ± 239.2	**<0.01**
% IMAT (Intra Muscolar Adipose Tissue)	2.207 ± 0.385	2.093 ± 0.451	**<0.05**
AT (Adipose Tisssue) (Kg)	44.76 ± 15.44	42.51 ± 15.60	**<0.01**

Table 10b. Body composition changes after 24 weeks of combined training. Parameters were acquired with BIA-ACC Medical Device (Biotekna s.r.l., Italy). Significance was set at $p< 0.05$. Differently from other parameters, Bone, T-score, Muscle and S-score do not show significant changes after 24 weeks of training.

BODY COMPOSITION IN THE WHOLE SAMPLE AFTER 12 WEEKS OF DETRAINING

PARAMETER	BASELINE	AFTER 24 WEEKS OF TRAINING	AFTER 12 WEEKS OF DETRAINING	Friedman Test p value	Dunn's Post (after 24 weeks of training vs after 12 weeks o detrainng) p value
BMI (Kg/m^2)	31.65 ± 4.579	30.799 ± 4.533	31.03 ± 4.172	=0.125	ns
%TBW (total body water)	39.96 ± 3.906	**42.08 ± 4.085**	**40.75 ± 4.225**	**<0.0001**	**<0.01**
%FFM (free fat mas)	59.58 ± 4.924	**61.38 ± 5.323**	**60.46 ± 5.283**	**<0.0001**	**<0.01**
%FM (fat mas)	40.42 ± 4.942	**38.63 ± 5.323**	**39.54 ± 5.283**	**<0.0001**	**<0.01**
BMR (basal metabolic rate)(kcal/die)	1449 ± 119.0	1474 ± 112.2	14567 ± 120.2	**<0.01**	ns
Body Density (g/cm^3)	1.006 ± 0.0089	**1.010 ± 0.011**	**1.008 ± 0.011**	**<0.0001**	**<0.01**
Bone (kg)	3.82± 0.656	3.99 ± 0.600	3.89 ± 0.689	**<0.0001**	ns
T-Score	-0.237 ± 0.691	-0.03± 0.634	-0.14± 0.612	**<0.0001**	ns
Muscle (kg)	19.36 ± 4.20	20.05 ± 3.996	19.64 ± 4.156	**<0.0001**	ns
S-score	1.183 ± 1.056	1.413 ± 1.033	1.179 ± 0.852	**<0.0001**	ns
AAT (addominal adipose tissue) (cm^2)	583.8 ± 211.0	**553.1 ± 209.1**	**571.9 ± 201.5**	**<0.0001**	**<0.01**
% IMAT (Intra Muscolar Adipose Tissue)	2.213 ± 0.365	2.117 ± 0.357	2.146 ± 0.414	**<0.0001**	ns
AT (Adipose Tisssue) (Kg)	43.68 ± 13.60	**41.51 ± 13.65**	**42.56 ± 13.42**	**<0.01**	**<0.01**

Table 11. Body composition changes after 12 weeks of detraining in the whole sample. Parameters were acquired with BIA-ACC Medical Device (Biotekna s.r.l., Italy). Significance was set at $p< 0.05$. TBW, Body density and FFM showed a significant decrease in 12 weeks of detraining while FM, AAT and AT increased.

Correlations

Spearman's correlation was utilized to verify if cardiovascular variables were related to anthropometrics and body composition parameters. A strong correlation was detected between Abdominal Adipose Tissue (AAT) and Diastolic Blood Pressure (DPB) (r= 0.56; p< 0,001, Figure 1), BMI and Pulse Wave Velocity (PWV) (r= 0.57; p< 0.001, Figure 2) and ABPM DBP daytime and waist circumference (r= 0.58; p<0.001 Figure 3). Furthermore, moderate correlation was identified between HOMA-index and ABPM DBP daytime (r= 0.6; p<0,01, Figure 4) and central SBP and Adipose Tissue (r=0.55; p< 0,01, Figure 5).

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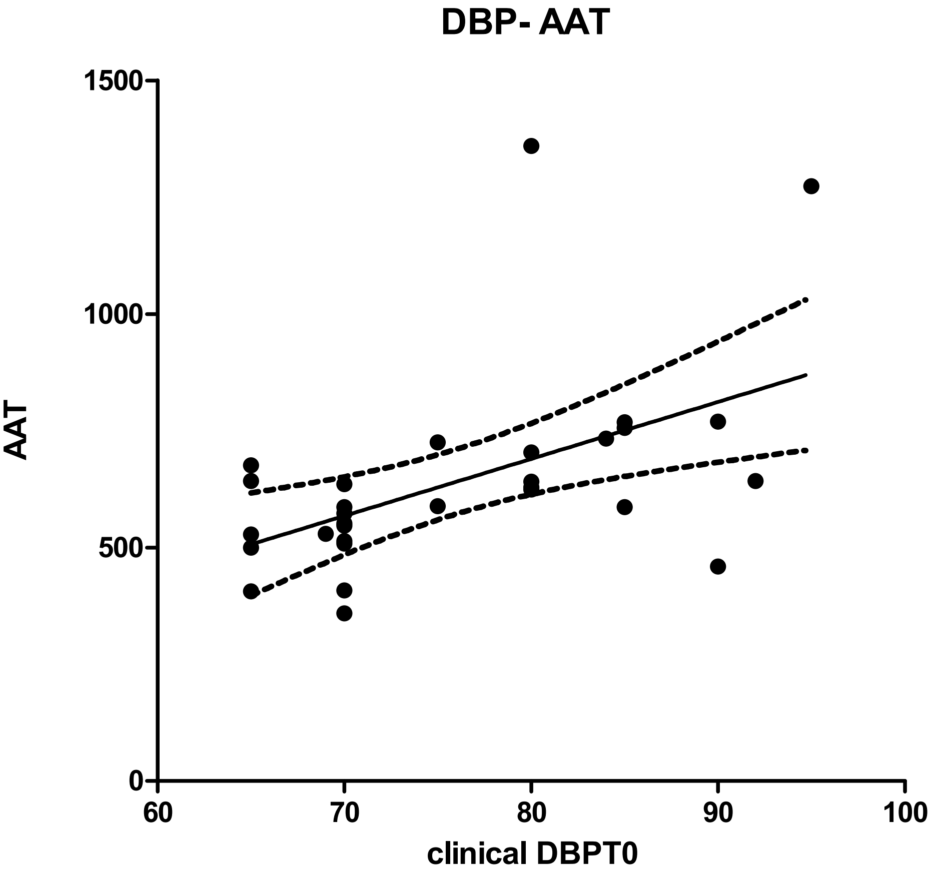

Figure 1. Correlation between AAT and clinical DBP at baseline. A strong correlation was found between these two variables (r= 0.56; p< 0,001).

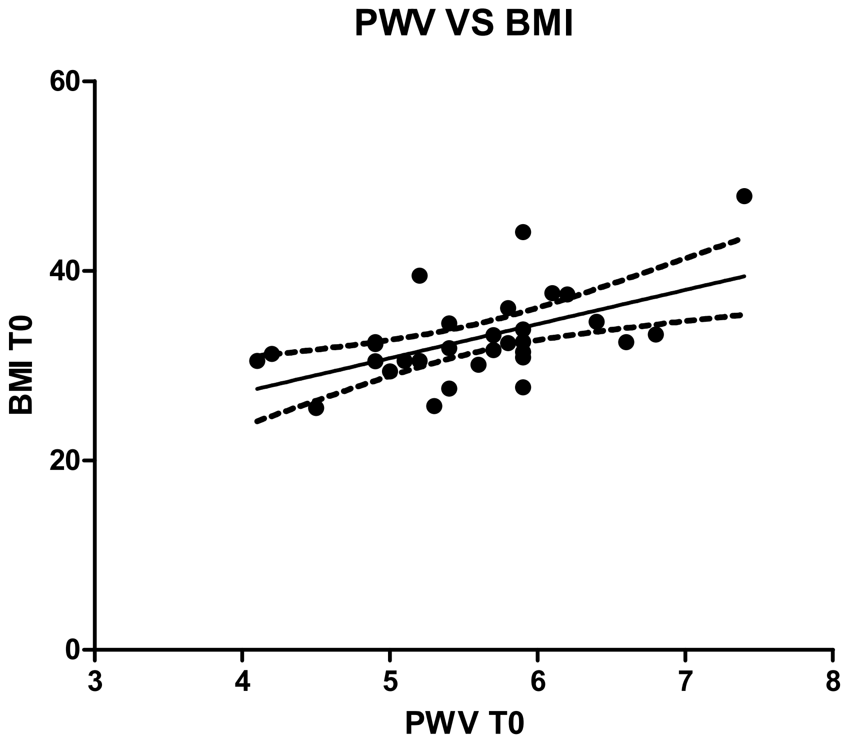

Figure 2. Correlation between BMI and PWV at baseline. A strong correlation was found between these two variables (r= 0.57; p< 0,001).

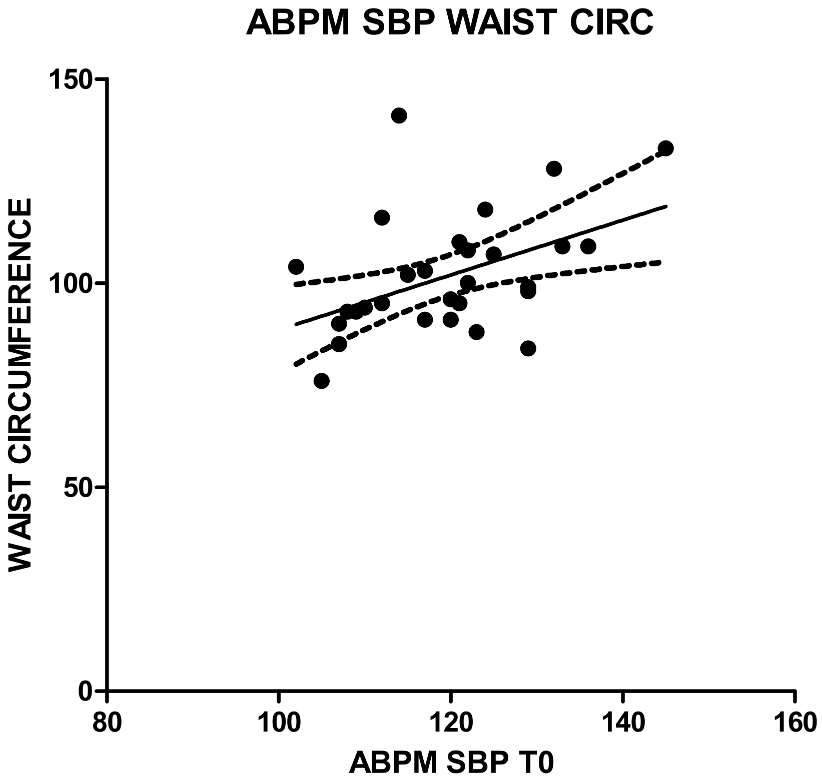

Figure 3. Correlation between Waist circumference and ABPM SBP at baseline. A strong correlation was found between these two variables (r= 0.58; p< 0,001).

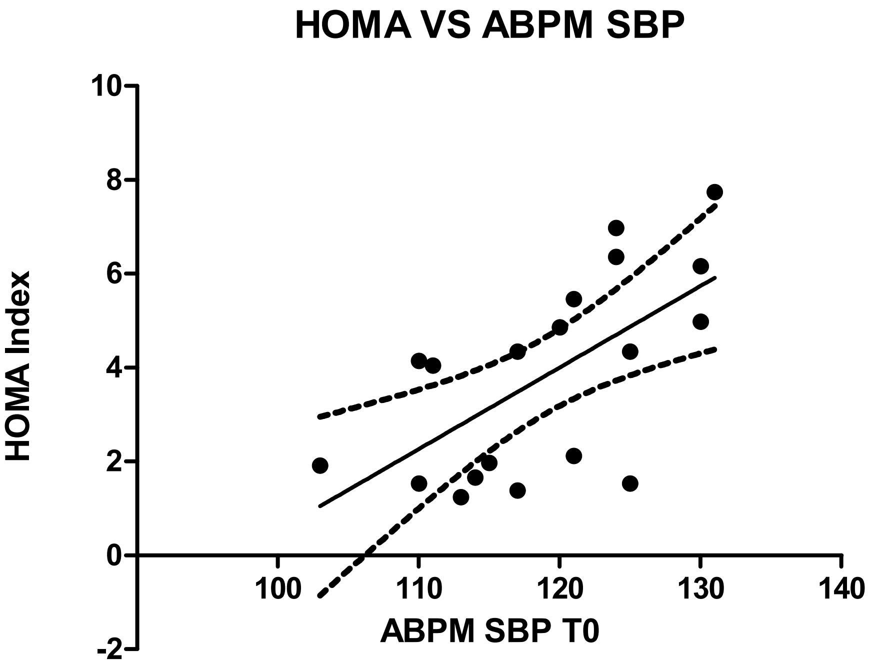

Figure 4. Correlation between HOMA-Index and ABPM SBP at baseline. A moderate correlation was found between these two variables (r= 0.60; p< 0,01).

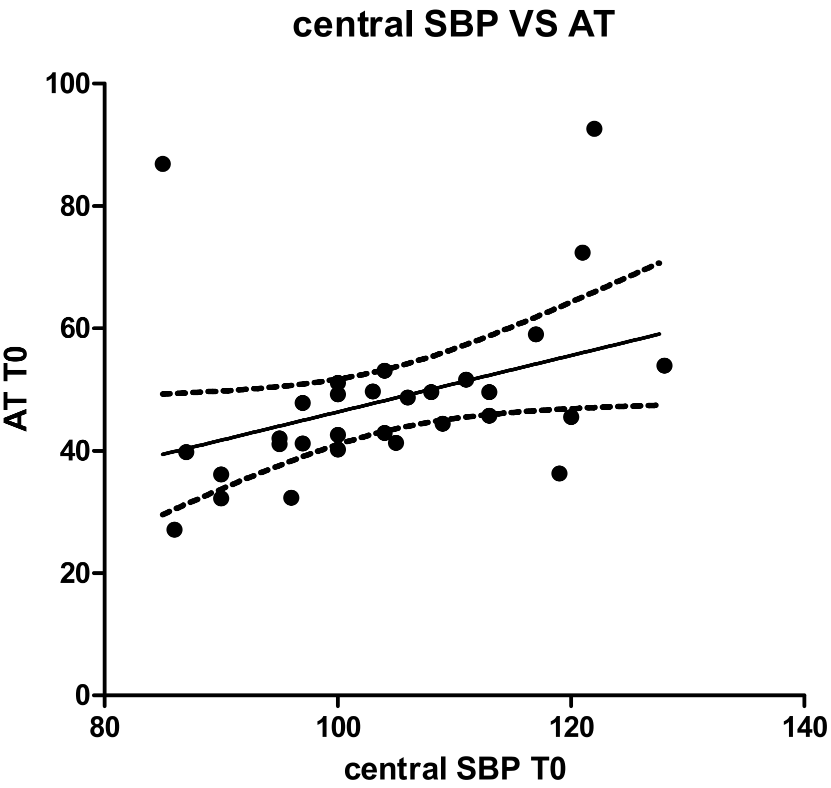

Figure 5. Correlation between AT and central SBP at baseline. A moderate correlation was found between these two variables (r= 0.55; p< 0,01).

DISCUSSION

The findings of this study provide interesting information regarding the role of physical activity in the prevention and treatment of obesity. As know, obesity is a big problem of our industrialized society, in particular when related to children and adolescents [106]. Obesity in "teenage" can affect cardiovascular and metabolic profile causing hypertension, reducing HRV and promote insulin-resistance [107]–[109]. Therefore, exercises has been suggested as a powerful mean to reduce fat mass, provide insulin-sensitivity and improve cardiovascular health [88], [110], [111]. In the present study a significant reduction of diastolic blood pressure and heart rate was identified after 24 weeks of physical activity. This outcome agrees with literature where it is reported that physical exercise has the power to improve cardiovascular profile of obese and/or hypertensive people [89], [112]. The most interesting aspect of this outcome is that these results has been reached independently from type of physical activity. Even if aerobic or endurance exercise is usually preferred to resistance one in the management and prevention of obesity and/or hypertension [113], resistance training has also a great power in improving cardiovascular and metabolic profile [95]. It was demonstrated as supervised resistance training can be very helpful to reduce and manage cardiovascular diseases and obesity [114]. However, resistance training is not as easy to incorporate into people's daily routine. Liu and colleagues [115] reported that it is easier to involve people to practise aerobic activities such as walking or biking than weightlifting. On the opposite, considering benefits that resistance training can provide, this study suggests people to utilize resistance training in the management of obesity, taking in account that this activity has also a captivating power on young people [96].

As regards metabolic profile, a significant decrease of blood triglycerides was found in the whole sample after 24 weeks of training. In addition, it was detected a trend to increase ($p=0.067$) in values of HDL and reducing blood sugar ($p=0.070$). For that it concern HDL values, this finding are conformed to literature, where studies declare the importance of physical activity in reducing triglycerides and increasing HDL [116], [117]. On the other hand, blood sugar showed a trend to decrease, even if not significant. This outcome is conform to the findings of Teh and colleagues [118] about the power of physical activity in reducing blood sugar. The reason why we noticed only a trend in the growth of HDL and reduction of blood sugar might be led to the sample size. Differently from studies where it was found a significant increase of HDL [116]–[118], our sample is smaller. Thus, this is a possible reason why we detected only a trend and not a significant difference as cited authors reported. However, this trend is very important if it is consider that higher levels of HLD has been identified as a preventive factor for metabolic syndrome [119]. Therefore, this study shows and confirm the role of physical activity as a non-pharmacological treatment in the management of obesity and metabolic syndrome. Unfortunately, we were not able to discriminate how the two types of physical activity influenced metabolic profile. A systematic review of Escalante and colleagues [117] underline as combined training can improve HDL concentrations while pure aerobic (endurance) training improves LDL cholesterol and triglycerides values. We found a similar behaviour of metabolic profile in our combined and resistance training group but without a significative difference. According to Gordon and colleagues [120], resistance training can help in reducing triglycerides and increase HDL as combined and aerobic training do. Thus, even if we found a significant difference only when the whole sample was analysed, this study seems to confirm the power of physical activity in improving metabolic profile of obese people.

Concerning body composition, strong differences were identified between the whole sample and a reference group of healthy adolescents of the same age, except in resting metabolic rate (BMR) ($p=0.725$), bone and muscle mass ($p=0.282$ and 0.646 respectively). Result on BMR are in accordance with Dal and colleagues [121] who found that resting energy expenditure is similar in obese and normal weight people. Moreover, bone and muscle mass increase if stimulated by training. A review of Damas and colleagues [122] shows as resistance training induced changes in skeletal muscle protein synthesis and, consequently, contribute to hypertrophy. Reference group was composed by healthy and active adolescents but not athletes. Thus, even if healthy, without a specific training it is not possible to gain muscle and bone mass. For this reason, we do not identify differences between the whole sample and reference group at baseline. Conversely, Fat Mass, BMI, Adipose Tissue, Abominal Adopise Tissue, Intra Muscolar Adopose Tissue and body density were strongly different in favour of reference group ($p< 0.001$). Alterations in this parameters are discriminant in the diagnosis of obesity and OSO [13], [40]. As previously reported, OSO raise when a strong impairment between muscle, bone and fat mass occurs in favour of fat mass (T-score and S-score are below 2 standard deviation from normality). Fortunately, we did not identify any participant being in OSO during this study, even this condition can appear in young people associated with other metabolic diseases [42].

On the opposite, no differences were detected at baseline between Resistance Training and Combined Training at baseline. It means that both groups started training with the same body composition profile.

After 24 weeks of training, both groups strongly improved most of the parameters of body composition expect BMI in Resistance Training ($p=0.255$) and Bone, T-score, Muscle and S-score in Combined Training group ($p=0.086$; 0.093; 0.363; 0.914 respectively). Stagnation of BMI in Resistant Training is maybe due to the insight property of this kind of training. As previously reported [93], [122] resistance training induced changes in skeletal muscle protein enhancing hypertrophy. Thus, Muscle mass and Fat Free Mass increase replacing Fat Mass. Consequently, total body weight does not change but its components were modified in favour of Fat Free Mass. Considering that BMI is calculated from height and body weight, if body weight does not change, BMI will remain the same too. On the opposite, Resistance Training has significantly improved parameters of Bone, T-score, Muscle and S-score ($p<0.01$) while combined training does not. With this study we confirm what in literature was previously reported [93], [122]. Resistance Training improved significantly Muscle and Bone stimulating it through insight properties of this kind of training. On the opposite, combined training was not able to improve these variables. Nevertheless, these findings are in accordance with Yan and Colleagues [123] that declared how only resistance training can enhance Muscle and Bone mass while aerobic does not. Differently from them, we utilized a combined training instead of a pure aerobic (endurance) one but the “resistance component “contained in this program was not strong enough to provoke changes in Muscle and Bone mass. Therefore, stasis in Muscle and Bone values in combined training proposed in this study suggest that this kind of training can maintain parameters avoiding a decrease of values of Muscle and Bone mass. For the same reason, combined training decreased significantly BMI values. That is due to the “aerobic component” of this kind of training [124]. Contrary to “resistance component”, the aerobic one is strong enough to allow a fat reduction. Considering that muscle and bone does not change, a total body weight reduction can arise influencing BMI ($p<0.05$). Enhancing or maintaining bone and muscle mass together with a reduction of BMI honours physical activity with a key role in the prevention and management of obesity and OSO.

Adipose Tissue (AT), Abdominal Adipose Tissue (AAT) and Intra Muscolar Adipose Tissue (IMAT) were significantly reduced in both groups ($p<0.001$). Therefore, both training efficaciously influenced these variables. AAT and IMAT are related with cardiovascular diseases onset and increased risk of death [51], [125]. Consequently, these findings empower the role of physical activity in the prevention of cardiovascular diseases and in their management. No differences were identified between groups in these three variables. Therefore, both resistance and combined training may be considered efficient in fat reduction in a young obese population.

BMR and Body density increased significantly after 24 weeks of training in both groups ($p<0.01$ for body density in both groups; $p< 0.01$ for BMR in resistance training; $p< 0.05$ for BMR in combined training). Logically, when Free Fat Mass (FFM) and muscle growth occurs it would be right to think that also energy needed to maintain body alive should increase. However, our findings disagree with the study of Alberga and colleagues and Miller and colleagues [126], [127] who did not find changes in BMR after resistance training but is in accordance with Cardoso and colleagues [128] that, conversely, identified improvements in BMR after resistance training. Miller and colleagues [127] analysed results on a period of four months of activity with indirect calorimetry acquired from DEXA, while Alberga and colleagues' outcomes [126] where acquired over a period of 22 weeks and BMR was directly calculated. The reason why our findings disagree with these two researches may lay on the study length in the case of Miller and colleagues (16 weeks vs 24 of our study) and in the BMR measurement for that it concerns Alberga and colleagues' results. We analysed BMR indirectly through BIA-ACC device while Alberga and colleagues calculated through respiratory exchanges analysis. However, the study of Cardoso and colleagues [128] measured BMR analysing oxygen consumption (VO_2) and carbon dioxide production (VCO_2) and claims that BMR can significantly increase after resistance training in obese women confirming our findings. This disagreement on BMR effects of resistance training might be elicited from workout intensity. Both Alberga and colleague and Miller and colleagues [126], [127] does not increase intensity (in terms of amount of lifted load) during their researches period. On the opposite, this study and the research of Cardoso gradually increased workout intensity. This fact probably guided to different outcomes on BMR.

For that in concern body density, a significant increase was identified after 24 weeks of training in both groups ($p<0,01$). This outcome confirm and enhance the role of physical activity in changing body composition and increasing body density [129]. Body density can be represented as the quotient of mass divided by volume. Body fat has a density of 0.90, while the density of fat free body mass is 1.10. Determination of density by measuring body volume and weight, permits calculation of the proportions of fat and lean body tissue. Thus, the more body density is near to 1.10, the higher and efficient the Fat Free Mass will be.

Finally, Total Body Water (TBW) increased significantly in both training groups. Water is an extremely important component of every bodily function such as digestion, transporting nutrients, lubricates brain and joint tissue, eliminate waste from cells and regulate body temperature. Consequently, hydration is a key process to remain healthy and efficient. Usually obese people are less hydrated than active one. They drink less and are less efficient that normal- weight [130]. Physical activity was identified as a good tool to help people increase their levels of hydration. In particular, Ribeiro and colleagues [131] showed as resistance training can be a good tool to increase TBW both in men and women. Our findings confirm this trend underlining again the role of physical activity in restoring body efficacy. In addition, we demonstrated that combined training can produce the same effects as resistance one on TBW. Consequently, TBW is altered indipendenlty from the type of physical activity.

Finally, we investigated correlations between cardiovascular, metabolic and body composition variables. We detected a strong correlation between Abdominal Adipose Tissue (AAT) and Diastolic Blood Pressure (DBP) ($r = 0.56$; $p < 0.001$), BMI and Pulse Wave Velocity (PWV) ($r = 0.57$; $p < 0.001$), ABPM SBP and Waist circumference ($r = 0.60$; $p < 0.001$). In addition, moderate correlations were found between Homa Index and ABPM SBP ($r = 0.6$; $p = 0.003$) and central SBP and Adipose Tissue (AP) ($r = 0.55$; $p = 0.002$).

This study confirms the existent connection between AAT and alteration in cardiovascular system. As previously reported, [51] abdominal obesity is related with an increased risk of low grade inflammation [132], heart failure and death. However, after the 24 weeks of training purposed in this research both groups reduced AAT. Consequently, findings of this study reinforce the role of physical activity in preventing cardiovascular diseases due to an excess of abdominal fat.

This study reveals that Pulse Wave Velocity (PWV) is strictly connected with BMI. As previously reported, BMI is related to fat mass [13] and PWV seems to be related to body fat [133]. Consequently, our findings suggest that higher levels of BMI are potentially risky for cardiovascular health.

The same relationship was identified by this study between ABPM SBP and waist circumferences. Therefore, higher values of waist circumference can warn that cardiovascular health can be compromised. BMI and waist circumference are two diagnostic tools very easy to be acquire, so they can be use on a large scale as a first screening in order to manage cardiovascular risk in obese people. The relationship between body composition and cardiovascular profile is strengthened by the correlation found in this study within SBP and AT. Moreover, the correlation between ABPM SPB and Homa-index suggests as cardiovascular and metabolic profile are connected. Therefore, human body changes its cardiovascular and metabolic profile when insight properties are altered, and modifications in body compositions affects cardiovascular and metabolic systems [134]. In conclusion, this research highlights the role of physical activity in modifying body composition, and, consequently, cardiovascular and metabolic profile despite of diet. Adherence to dietary advices was very poor, so physical activity played an important role in determining our outcomes.

Limitations

There may be some possible limitations in this study. First, the sample size can be considered the greatest one. This study was conducted in an ecological environment, so people were asked to modify their daily routine and investing time in physical activity. The difficulty in involving and motivating obese adolescents in physical activity is a strong limiting factor in recruiting participants. In addition, these boys and girls usually have low school performances. For this reason, parents hardly encourage their children to spend time in activities that are different from studying and accomplish school assignments. Moreover, it is not so easy to insert a new activity in the daily routine, so the risk of rejecting the physical activity purpose is tangible. Finally, the recruitment was done in hospital after clinical evaluation. However, a lot of obese people and their family do not or do not want to recognize their status. Consequently, a great potential sample could not be involved in the study.

Secondly, adherence to dietary advices may be affected results limiting the study potential. Probably, with a restricted diet and a clinical diet monitoring effects on body composition, metabolic and cardiovascular profile would be empowered and increased. The facts of being in their “real world” permitted them to have access to all kind of food and lifestyles that may affected results. On the other hand, the ecological environment in which the study was done could represent a great chance to register data coming from “the real life” and shows what effectively could be the role of physical activity in managing youth obesity.

Finally, another limitation may be identified in the exercise’s intensity. Even if intensity increased during the 24 weeks of training, participants where all beginners and they need to learn how to train and training to train themselves. A more intense training program might provide greater effects, but beginners needed to be educated before increasing training intensity.

CONCLUSIONS

Overweight and obese adolescents are at risk for significant health problems both during their youth and as adults. Their condition exposes them to higher risk factors associated with cardiovascular disease and insulin resistance (e.g. high blood pressure, high cholesterol and type 2 diabetes mellitus) and to develop an early form of OSO. Physical activity is one of the most powerful and non-pharmacological treatment to manage and prevent this medical condition. Even if the sample size was small, results from this study have demonstrated the role of physical activity in improving cardiovascular, metabolic profile and promoting changes in body compositions. Resistance and combined training were both efficient in improving health profile of obese adolescents. Resistance training is associated with an increase of muscle and bone mass but without a decrease in BMI while combined training leads to a decrease of BMI but no increments in bone and muscle mass. Despite this, both are efficient in reducing fat mass, blood pressure and improve the metabolic profile emphasizing the importance of prescribe and suggest physical activity in obese adolescents. These outcomes reinforce the benefits of resistance training confirming is potential in re-modelling body composition by affecting muscle, bone and fat mass and reveal as combined training is useful in reducing BMI and fat mass in a population of obese adolescents.

REFERENCES

[1] J. R. Sowers, “Obesity as a cardiovascular risk factor,” *Am. J. Med.*, vol. 115, no. 8 SUPPL. 1, pp. 37–41, 2003.

[2] M. I. Goran, G. D. C. Ball, and M. L. Cruz, “Cardiovascular endocrinology 2: Obesity and risk of type 2 diabetes and cardiovascular disease in children and adolescents,” *J. Clin. Endocrinol. Metab.*, vol. 88, no. 4, pp. 1417–1427, 2003.

[3] W. P. T. J. David W Haslam, “Obesity,” *Lancet*, pp. 1197–1209, 2005.

[4] K.-B. A. and W. M.L., “Health economics of weight management: Evidence and cost,” *Asia Pac. J. Clin. Nutr.*, vol. 16, no. SUPPL.1, pp. 329–338, 2007.

[5] M. L. Specchia *et al.*, “Economic impact of adult obesity on health systems: A systematic review,” *Eur. J. Public Health*, vol. 25, no. 2, pp. 255–262, 2015.

[6] B. Caballero, “The global epidemic of obesity: An overview,” *Epidemiol. Rev.*, vol. 29, no. 1, pp. 1–5, 2007.

[7] T. Roenneberg, K. V. Allebrandt, M. Merrow, and C. Vetter, “Social jetlag and obesity,” *Curr. Biol.*, vol. 22, no. 10, pp. 939–943, 2012.

[8] M. Adela Hruby, PhD and M. Frank B. Hu, MD, PhD, “The Epidemiology of Obesity: A Big Picture,” *Pharmacoeconomics.*, vol. 33, no. 7, pp. 673–689, 2015.

[9] J. Sobal and A. J. Stunkard, “Socioeconomic Status and Obesity: A Review of the Literature,” *Psychol. Bull.*, vol. 105, no. 2, pp. 260–275, 1989.

[10] S. W. Keith *et al.*, “Putative contributors to the secular increase in obesity: Exploring the roads less traveled,” *Int. J. Obes.*, vol. 30, no. 11, pp. 1585–1594, 2006.

[11] L. McLaren, “Socioeconomic status and obesity,” *Epidemiol. Rev.*, vol. 29, no. 1, pp. 29–48, 2007.

[12] B. Marcheva *et al.*, “Disruption of the clock components CLOCK and BMAL1 leads to hypoinsulinaemia and diabetes.,” *Nature*, vol. 466, no. 7306, pp. 627–631, 2011.

[13] D. S. Freedman and B. Sherry, “The validity of BMI as an indicator of body fatness and risk among children,” *Pediatrics*, vol. 124, no. SUPPL. 1, 2009.

[14] E. Di Angelantonio *et al.*, “Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents,” *Lancet*, vol. 388, no. 10046, pp. 776–786, 2016.

[15] L. H. Mortensen, I. C. Siegler, J. C. Barefoot, M. Grønbæk, and T. I. A. Sørensen, “Prospective associations between sedentary lifestyle and BMI in midlife,” *Obesity*, vol. 14, no. 8, pp. 1462–1471, 2006.

[16] F. Q. Nuttall, “Body Mass Index Obesity, BMI, and Health: A Critical Review,” *Nutr. Res.*, vol. 50, no. 3, 2015.

[17] B. Sciences, “Body Mass Index as a Predictor of Percent Fat in College Athletes and Nonathletes,” pp. 403–409, 2007.

[18] B. S. Nickerson *et al.*, “Validity of BMI-based body fat equations in men and women:

A 4-compartment model comparison," *J. Strength Cond. Res.*, vol. 32, no. 1, pp. 121–129, 2018.

[19] J. A. Shepherd, B. K. Ng, M. J. Sommer, and S. B. Heymsfield, "Body composition by DXA," *Bone*, vol. 104, pp. 101–105, 2017.

[20] J. Galgani and E. Ravussin, "Energy metabolism, fuel selection and body weight regulation," *Int. J. Obes.*, vol. 32, no. SUPPL. 7, pp. 109–119, 2008.

[21] J. Z. Ilich, O. J. Kelly, and J. E. Inglis, "Osteosarcopenic Obesity Syndrome: What Is It and How Can It Be Identified and Diagnosed?," *Curr. Gerontol. Geriatr. Res.*, vol. 2016, no. Figure 1, pp. 1–7, 2016.

[22] J. C. K. Wells and M. S. Fewtrell, "Measuring body composition," *Arch Dis Child*, pp. 612–617, 2006.

[23] H. S. Wang ZM, Pierson RN Jr, "The five-level model : a new approach to organizing," *Am J Clin Nutr.*, 1991.

[24] S. B. Heymsfield *et al.*, "Chemical and elemental analysis of humans in vivo using improved body composition models," *Am. J. Physiol. - Endocrinol. Metab.*, vol. 261, no. 2 24-2, 1991.

[25] K. N. F. Michael I. Gurr, John L. Harwood, *Lipid Biochemistry - An Introduction*. 2002.

[26] M. Peppa, C. Stefanaki, A. Papaefstathiou, D. Boschiero, G. Dimitriadis, and G. P. Chrousos, "Bioimpedance analysis vs. DEXA as a screening tool for osteosarcopenia in lean, overweight and obese Caucasian postmenopausal females," *Hormones*, vol. 16, no. 2, pp. 181–193, 2017.

[27] F. Li *et al.*, "Anthropometric measurement standardization in the US-affiliated pacific: Report from the Children's Healthy Living Program," *Am. J. Hum. Biol.*, vol. 28, no. 3, pp. 364–371, 2016.

[28] Y. Lahav, Y. Epstein, R. Kedem, and H. Schermann, "A novel body circumferences-based estimation of percentage body fat," *Br. J. Nutr.*, vol. 119, no. 6, pp. 720–725, 2018.

[29] A. Berger, "Bone mineral density scans," *Bmj*, vol. 325, no. 7362, p. 484, 2002.

[30] P. Pisani, "Screening and early diagnosis of osteoporosis through X-ray and ultrasound based techniques," *World J. Radiol.*, vol. 5, no. 11, p. 398, 2013.

[31] J. L. Bone, M. L. Ross, K. A. Tomcik, N. A. Jeacocke, W. G. Hopkins, and L. M. Burke, "Manipulation of Muscle Creatine and Glycogen Changes Dual X-ray Absorptiometry Estimates of Body Composition," *Med. Sci. Sports Exerc.*, vol. 49, no. 5, pp. 1029–1035, 2017.

[32] A. Bazzocchi, F. Ponti, U. Albisinni, G. Battista, and G. Guglielmi, "DXA: Technical aspects and application," *Eur. J. Radiol.*, vol. 85, no. 8, pp. 1481–1492, 2016.

[33] A. M. Silva *et al.*, "Do dynamic fat and fat-free mass changes follow theoretical driven rules in athletes?," *Med. Sci. Sports Exerc.*, vol. 49, no. 10, pp. 2086–2092, 2017.

[34] M. Dehghan and A. T. Merchant, "Is bioelectrical impedance accurate for use in large epidemiological studies?," *Nutr. J.*, vol. 7, no. 1, pp. 1–7, 2008.

[35] D. A. Baur, C. W. Bach, W. J. Hyder, and M. J. Ormsbee, "Fluid retention, muscle

damage, and altered body composition at the Ultraman triathlon," *Eur. J. Appl. Physiol.*, vol. 116, no. 3, pp. 447–458, 2016.

[36] G. H. Goossens, "The Metabolic Phenotype in Obesity: Fat Mass, Body Fat Distribution, and Adipose Tissue Function. Obes Facts. 2017;10(3):207–15. The Metabolic Phenotype in Obesity: Fat Mass, Body Fat Distribution, and Adipose Tissue Function," *Obes. Facts*, vol. 10, no. 3, pp. 207–215, 2017.

[37] M. B. Snijder, P. Z. Zimmet, M. Visser, J. M. Dekker, J. C. Seidell, and J. E. Shaw, "Independent and opposite associations of waist and hip circumferences with diabetes, hypertension and dyslipidemia: The AusDiab Study," *Int. J. Obes.*, vol. 28, no. 3, pp. 402–409, 2004.

[38] S. Yusuf *et al.*, "Obesity and the risk of myocardial infarction in 27 000 participants from 52 countries: A case-control study," *Lancet*, vol. 366, no. 9497, pp. 1640–1649, 2005.

[39] R. Roubenoff, "Sarcopenic obesity: The confluence of two epidemics," *Obes. Res.*, vol. 12, no. 6, pp. 887–888, 2004.

[40] J. Z. Ilich, O. J. Kelly, J. E. Inglis, L. B. Panton, G. Duque, and M. J. Ormsbee, "Interrelationship among muscle, fat, and bone: Connecting the dots on cellular, hormonal, and whole body levels," *Ageing Res. Rev.*, vol. 15, no. 1, pp. 51–60, 2014.

[41] M. J. Ormsbee *et al.*, "Osteosarcopenic obesity: the role of bone, muscle, and fat on health," *J. Cachexia. Sarcopenia Muscle*, vol. 5, no. 3, pp. 183–192, 2014.

[42] C. Stefanaki, M. Peppa, D. Boschiero, and G. P. Chrousos, "Healthy overweight/obese youth: early osteosarcopenic obesity features," *Eur. J. Clin. Invest.*, vol. 46, no. 9, pp. 767–778, 2016.

[43] and N. K. JOHN A. KANIS, L. JOSEPH MELTON, 111, CLAUS CHRISTIANSEN, CONRAD C. JOHNSTON, "The diagnosis of osteoporosis," *J. Bone Miner. Res.*, vol. 9, no. 8, pp. 1137–1141, 1994.

[44] A. J. Cruz-Jentoft *et al.*, "Sarcopenia: European consensus on definition and diagnosis," *Age Ageing*, vol. 39, no. 4, pp. 412–423, 2010.

[45] P. Poirier *et al.*, "Obesity and cardiovascular disease: Pathophysiology, evaluation, and effect of weight loss: An update of the 1997 American Heart Association Scientific Statement on obesity and heart disease from the Obesity Committee of the Council on Nutrition, Physical," *Circulation*, vol. 113, no. 6, pp. 898–918, 2006.

[46] M. Imo A. Ebong, MD, MS, David C. Goff Jr, MD, PhD, Carlos J. Rodriguez, MD and M. Haiying Chen, PHD, and Alain G. Bertoni, MD, "Mechanisms of Heart Failure in Obesity," vol. 27, no. 4, pp. 1–14, 2014.

[47] M. J. Buscot *et al.*, "Distinct child-to-adult body mass index trajectories are associated with different levels of adult cardiometabolic risk," *Eur. Heart J.*, vol. 39, no. 24, pp. 2263-2270a, 2018.

[48] A. J. Foy, J. Mandrola, G. Liu, and G. V. Naccarelli, "Relation of Obesity to New-Onset Atrial Fibrillation and Atrial Flutter in Adults," *Am. J. Cardiol.*, vol. 121, no. 9, pp. 1072–1075, 2018.

[49] M. Packer, "Epicardial Adipose Tissue May Mediate Deleterious Effects of Obesity and Inflammation on the Myocardium," *J. Am. Coll. Cardiol.*, vol. 71, no. 20, pp. 2360–2372, 2018.

[50] T. Tsujimoto, H. Kajio, and M. Packer, “Abdominal Obesity Is Associated With an Increased Risk of All-Cause Mortality in Patients With HFpEF,” *J. Am. Coll. Cardiol.*, vol. 71, no. 22, pp. 2360–2372, 2017.

[51] T. Tsujimoto, H. Kajio, and M. Packer, “Abdominal Obesity Is Associated With an Increased Risk of All-Cause Mortality in Patients With HFpEF,” *J. Am. Coll. Cardiol.*, vol. 71, no. 22, pp. 2360–2372, 2017.

[52] M. Packer, “Epicardial Adipose Tissue May Mediate Deleterious Effects of Obesity and Inflammation on the Myocardium,” *J. Am. Coll. Cardiol.*, vol. 71, no. 20, pp. 2360–2372, 2018.

[53] Rainer H. Straub, *The Origin of Chronic Inflammatory Systemic Diseases and their Sequelae*. 2015.

[54] W. Zhang and N. Li, “Prevalence, risk factors, and management of prehypertension,” *Int. J. Hypertens.*, vol. 2011, pp. 1999–2000, 2011.

[55] H. M. Shihab *et al.*, “Body Mass Index and Risk of Incident Hypertension Over The Johns Hopkins Precursors Study,” *Circulation*, pp. 2983–2989, 2012.

[56] P. W. F. Wilson, R. B. D. Agostino, L. Sullivan, H. Parise, and W. B. Kannel, “Overweight and Obesity as Determinants of Cardiovascular Risk,” *Arch Intern Med.*, vol. 162, pp. 1865–1872, 2002.

[57] J. P. Forman, M. J. Stampfer, and G. C. Curhan, “Diet and Lifestyle Risk Factors Associated With Incident Hypertension in Women,” *JAMA*, vol. 302, no. 4, pp. 401–411, 2009.

[58] E. Verrif, C. van Montfrans, and J. W. Bos, “Reintroduction of Riva-Rocci measurements to determine systolic blood pressure?,” *Neth. J. Med.*, vol. 66, no. 11, pp. 480–482, 2008.

[59] M. Thomas G. Pickering, MD, DPhil; John E. Hall, PhD; Lawrence J. Appel, MD; Bonita E. Falkner, M. John Graves, MD; Martha N. Hill, RN, PhD; Daniel W. Jones, MD; Theodore Kurtz, and M. Sheldon G. Sheps, MD; Edward J. Roccella, PhD, “Recommendations for Blood Pressure Measurements and Experimental Animals,” *Circulation*, vol. 74, no. 40, pp. 1372–1375, 2005.

[60] B. S. Alpert, D. Quinn, and D. Gallick, “Oscillometric blood pressure: A review for clinicians,” *J. Am. Soc. Hypertens.*, vol. 8, no. 12, pp. 930–938, 2014.

[61] A. L. Hinderliter, R. A. Voora, and A. J. Viera, “Implementing ABPM into Clinical Practice,” *Curr. Hypertens. Rep.*, vol. 20, no. 1, pp. 20–25, 2018.

[62] G. Mancia, M. Bombelli, G. Seravalle, and G. Grassi, “Diagnosis and management of patients with white-coat and masked hypertension,” *Nat. Rev. Cardiol.*, vol. 8, no. 12, pp. 686–693, 2011.

[63] S.-J. Hwang *et al.*, “Arterial stiffness and cardiovascular events: the Framingham Heart Study,” *Circulation*, vol. 121, no. 4, pp. 505–511, 2010.

[64] C. Vlachopoulos, K. Aznaouridis, M. F. O’Rourke, M. E. Safar, K. Baou, and C. Stefanadis, “Prediction of cardiovascular events and all-cause mortality with central haemodynamics: A systematic review and meta-analysis,” *Eur. Heart J.*, vol. 31, no. 15, pp. 1865–1871, 2010.

[65] L. G. Stéphane Laurent, Pierre Boutouyrie, Roland Asmar, Isabelle Gautier, Brigitte Laloux and A. B. Pierre Ducimetiere, “Aortic stiffness is an independent predictor of

stroke in hypertensive patients," *Hypertension*, vol. 100, no. 5, pp. 437–443, 2001.

[66] T. Sehestedt *et al.*, "Risk prediction is improved by adding markers of subclinical organ damage to SCORE," *Eur. Heart J.*, vol. 31, no. 7, pp. 883–891, 2010.

[67] P. M. Nilsson *et al.*, "Early vascular ageing in translation: From laboratory investigations to clinical applications in cardiovascular prevention," *J. Hypertens.*, vol. 31, no. 8, pp. 1517–1526, 2013.

[68] W. W. Nichols, S. J. Denardo, I. B. Wilkinson, C. M. McEniery, J. Cockcroft, and M. F. O'Rourke, "Effects of arterial stiffness, pulse wave velocity, and wave reflections on the central aortic pressure waveform," *J. Clin. Hypertens.*, vol. 10, no. 4, pp. 295–303, 2008.

[69] S. Laurent *et al.*, "Expert consensus document on arterial stiffness: Methodological issues and clinical applications," *Eur. Heart J.*, vol. 27, no. 21, pp. 2588–2605, 2006.

[70] R. Pini *et al.*, "Central But Not Brachial Blood Pressure Predicts Cardiovascular Events in an Unselected Geriatric Population. The ICARe Dicomano Study," *J. Am. Coll. Cardiol.*, vol. 51, no. 25, pp. 2432–2439, 2008.

[71] K. Mohammedi *et al.*, "Outpatient measurement of arterial stiffness in patients with type 2 diabetes and obesity," *J. Diabetes*, vol. 9, no. 3, pp. 237–242, 2017.

[72] N. Kulsum-Mecci, C. Goss, B. A. Kozel, J. M. Garbutt, K. B. Schechtman, and V. R. Dharnidharka, "Effects of Obesity and Hypertension on Pulse Wave Velocity in Children," *J. Clin. Hypertens.*, vol. 19, no. 3, pp. 221–226, 2017.

[73] L. M. Walter *et al.*, "Overweight and obese children with sleep disordered breathing have elevated arterial stiffness," *Sleep Med.*, vol. 48, pp. 187–193, 2018.

[74] A. N. Gurovich and R. W. Braith, "Pulse wave analysis and pulse wave velocity techniques: Are they ready for the clinic," *Hypertens. Res.*, vol. 34, no. 2, pp. 166–169, 2011.

[75] G. F. Mitchell *et al.*, "Aortic diameter, wall stiffness, and wave reflection in systolic hypertension," *Hypertension*, vol. 51, no. 1, pp. 105–111, 2008.

[76] N. A. Jatoi, A. Mahmud, K. Bennett, and J. Feely, "Assessment of arterial stiffness in hypertension: Comparison of oscillometric (Arteriograph), piezoelectronic (Complior) and tonometric (SphygmoCor) techniques," *J. Hypertens.*, vol. 27, no. 11, pp. 2186–2191, 2009.

[77] J. Nemcsik *et al.*, "Validation of arteriograph - A new oscillometric device to measure arterial stiffness in patients on maintenance hemodialysis," *Kidney Blood Press. Res.*, vol. 32, no. 3, pp. 223–229, 2009.

[78] G. F. Mitchell *et al.*, "Omapatrilat reduces pulse pressure and proximal aortic stiffness in patients with systolic hypertension: Results of the conduit hemodynamics of omapatrilat international research study," *Circulation*, vol. 105, no. 25, pp. 2955–2961, 2002.

[79] D. P. Casey, D. T. Beck, and R. W. Braith, "Progressive resistance training without volume increases does not alter arterial stiffness and aortic wave reflection," *Exp. Biol. Med.*, vol. 232, no. 9, pp. 1228–1235, 2007.

[80] A. N. Gurovich, D. T. Beck, and R. W. Braith, "Aortic pulse wave analysis is not a surrogate for central arterial pulse wave velocity," *Exp. Biol. Med.*, vol. 234, no. 11, pp. 1339–1344, 2009.

[81] J. E. Donnelly *et al.*, “Aerobic exercise alone results in clinically significant weight loss for men and women: Midwest exercise trial 2,” *Obesity*, vol. 21, no. 3, pp. 219–228, 2013.

[82] Jakicic, “Effect of exercise on 24-month weight loss maintenance in overweight women (Archives of Internal Medicine (2008) 168, 4, (1550-1559)),” *Arch. Intern. Med.*, vol. 168, no. 19, p. 2162, 2008.

[83] M. Rosenkilde, P. Auerbach, M. H. Reichkendler, T. Ploug, B. M. Stallknecht, and A. Sjödin, “Body fat loss and compensatory mechanisms in response to different doses of aerobic exercise-a randomized controlled trial in overweight sedentary males,” *Am. J. Physiol. - Regul. Integr. Comp. Physiol.*, vol. 303, no. 6, pp. 571–579, 2012.

[84] P. Wiklund, “The role of physical activity and exercise in obesity and weight management: Time for critical appraisal,” *J. Sport Heal. Sci.*, vol. 5, no. 2, pp. 151–154, 2016.

[85] B. Murray and C. Rosenbloom, “Fundamentals of glycogen metabolism for coaches and athletes,” *Nutr. Rev.*, vol. 76, no. 4, pp. 243–259, 2018.

[86] J. A. Hawley and J. J. Leckey, “Carbohydrate Dependence During Prolonged, Intense Endurance Exercise,” *Sport. Med.*, vol. 45, no. 1, pp. 5–12, 2015.

[87] D. S.- Sharon Plowman, *Exercise Physiology for Health Fitness and Performance*. 2017.

[88] G. P. Nassis *et al.*, “Aerobic exercise training improves insulin sensitivity without changes in body weight, body fat, adiponectin, and inflammatory markers in overweight and obese girls,” *Metabolism.*, vol. 54, no. 11, pp. 1472–1479, 2005.

[89] R. Cade *et al.*, “Effect of aerobic exercise training on patients with systemic arterial hypertension,” *Am. J. Med.*, vol. 77, no. 5, pp. 785–790, 1984.

[90] T. Okura, Y. Nakata, D. J. Lee, K. Ohkawara, and K. Tanaka, “Effects of aerobic exercise and obesity phenotype on abdominal fat reduction in response to weight loss,” *Int. J. Obes.*, vol. 29, no. 10, pp. 1259–1266, 2005.

[91] J. R. Speakman and C. Selman, “Physical activity and resting metabolic rate,” *Proc. Nutr. Soc.*, vol. 62, no. 3, pp. 621–634, 2003.

[92] W. R. Marcell TJ, Hawkins SA, “Leg strength declines with advancing age despite habitual endurance exercise in active older adults.,” *Journa Strenght Cond. Res.*, vol. 28, no. 2, pp. 504–13, 2014.

[93] B. J. Schoenfeld, D. Ogborn, and J. W. Krieger, “Effects of Resistance Training Frequency on Measures of Muscle Hypertrophy: A Systematic Review and Meta-Analysis,” *Sport. Med.*, vol. 46, no. 11, pp. 1689–1697, 2016.

[94] D. M. Croymans *et al.*, “Resistance training improves indices of muscle insulin sensitivity and β-cell function in overweight/obese, sedentary young men,” *J. Appl. Physiol.*, vol. 115, no. 9, pp. 1245–1253, 2013.

[95] E. C. De Sousa, O. Abrahin, A. L. L. Ferreira, R. P. Rodrigues, E. A. C. Alves, and R. P. Vieira, “Resistance training alone reduces systolic and diastolic blood pressure in prehypertensive and hypertensive individuals: Meta-analysis,” *Hypertens. Res.*, vol. 40, no. 11, pp. 927–931, 2017.

[96] N. Schranz, G. Tomkinson, N. Parletta, J. Petkov, and T. Olds, “Can resistance training change the strength, body composition and self-concept of overweight and

obese adolescent males? A randomised controlled trial," *Br. J. Sports Med.*, vol. 48, no. 20, pp. 1482–1488, 2014.

[97] M. Wewege, R. van den Berg, R. E. Ward, and A. Keech, "The effects of high-intensity interval training vs. moderate-intensity continuous training on body composition in overweight and obese adults: a systematic review and meta-analysis," *Obes. Rev.*, vol. 18, no. 6, pp. 635–646, 2017.

[98] Ms. David Moher, P. Kenneth F Schulz, Ds. Douglas G Altman, and for the C. Group*, "The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials," *Lancet*, vol. 357, pp. 1191–1194, 2001.

[99] M. Liu, Y. Li, F. F. Wei, L. Zhang, J. L. Han, and J. G. Wang, "Is blood pressure load associated, independently of blood pressure level, with target organ damage?," *J. Hypertens.*, vol. 31, no. 9, pp. 1812–1818, 2013.

[100] M. I. Goran, G. D. C. Ball, and M. L. Cruz, "Obesity and risk of type 2 diabetes and cardiovascular disease in children and adolescents," *J. Clin. Endocrinol. Metab.*, vol. 88, no. 4, pp. 1417–1427, 2003.

[101] R. B. Devereux *et al.*, "Echocardiographic assessment of left ventricular hypertrophy: Comparison to necropsy findings," *Am. J. Cardiol.*, vol. 57, no. 6, pp. 450–458, 1986.

[102] A. Mookerjee, A. M. Al-Jumaily, and A. Lowe, "Arterial pulse wave velocity measurement: Different techniques, similar results-implications for medical devices," *Biomech. Model. Mechanobiol.*, vol. 9, no. 6, pp. 773–781, 2010.

[103] M. Brzycki, "Strength Testing—Predicting a One-Rep Max from Reps-to-Fatigue," *J. Phys. Educ. Recreat. Danc.*, vol. 64, no. 1, pp. 88–90, 1993.

[104] H. Krysztofiak, M. Młyńczak, A. Folga, W. Braksator, and Ł. A. Małek, "Normal Values for Left Ventricular Mass in Relation to Lean Body Mass in Child and Adolescent Athletes," *Pediatr. Cardiol.*, vol. 40, no. 1, pp. 204–208, 2019.

[105] J. Elmenhorst, M. Hulpke-Wette, C. Barta, R. Dalla Pozza, S. Springer, and R. Oberhoffer, "Percentiles for central blood pressure and pulse wave velocity in children and adolescents recorded with an oscillometric device," *Atherosclerosis*, vol. 238, no. 1, pp. 9–16, 2015.

[106] M. H. Park, C. Falconer, R. M. Viner, and S. Kinra, "The impact of childhood obesity on morbidity and mortality in adulthood: A systematic review," *Obes. Rev.*, vol. 13, no. 11, pp. 985–1000, 2012.

[107] M. A. Alpert, "Obesity cardiomyopathy: Pathophysiology and evolution of the clinical syndrome," *Am. J. Med. Sci.*, vol. 321, no. 4, pp. 225–236, 2001.

[108] W. S. (The N. Giuseppe Mancia* (ESH Chairperson) (Italy) *et al.*, *2018 ESC / ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of*. 2018.

[109] M. L. Marcovecchio, A. Mohn, and F. Chiarelli, "Obesity and insulin resistance in children," *J. Pediatr. Gastroenterol. Nutr.*, vol. 51, no. SUPPL. 3, pp. 149–150, 2010.

[110] P. Poirier *et al.*, "Obesity and cardiovascular disease: Pathophysiology, evaluation, and effect of weight loss," *Arterioscler. Thromb. Vasc. Biol.*, vol. 26, no. 5, pp. 968–976, 2006.

[111] R. R. Wing *et al.*, “Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes,” *Diabetes Care*, vol. 34, no. 7, pp. 1481–1486, 2011.

[112] H. J. Kang, Y. S. Lee, D. S. Park, and D. H. Kang, “Effects of 12-week circuit weight training and aerobic exercise on body composition, physical fitness, and pulse wave velocity in obese collegiate women,” *Soft Comput.*, vol. 16, no. 3, pp. 403–410, 2012.

[113] A. Petridou, A. Siopi, and V. Mougios, “Exercise in the management of obesity,” *Metabolism.*, vol. 92, pp. 163–169, 2019.

[114] M. A. Williams *et al.*, “Resistance exercise in individuals with and without cardiovascular disease: 2007 update: A scientific statement from the American Heart Association Council on Clinical Cardiology and Council on Nutrition, Physical Activity, and Metabolism,” *Circulation*, vol. 116, no. 5, pp. 572–584, 2007.

[115] Y. Liu *et al.*, *Associations of Resistance Exercise with Cardiovascular Disease Morbidity and Mortality*, vol. 51, no. 3. 2019.

[116] M. Said, N. Lamya, N. Olfa, and M. Hamda, “Effects of high-impact aerobics vs. low-impact aerobics and strength training in overweight and obese women,” *J. Sports Med. Phys. Fitness*, vol. 57, no. 3, pp. 278–288, 2017.

[117] Y. Escalante, J. M. Saavedra, A. García-Hermoso, and A. M. Domínguez, “Improvement of the lipid profile with exercise in obese children: A systematic review,” *Prev. Med. (Baltim).*, vol. 54, no. 5, pp. 293–301, 2012.

[118] C. H. Teh *et al.*, “Association of physical activity with blood pressure and blood glucose among Malaysian adults: A population-based study Chronic Disease epidemiology,” *BMC Public Health*, vol. 15, no. 1, pp. 1–7, 2015.

[119] S. Özer, R. Yılmaz, N. Ö. Kazancı, E. Sönmezgöz, B. Altuntaş, and Y. E. Kuyucu, “Higher hdl levels are a preventive factor for metabolic syndrome in obese Turkish children,” *Nutr. Hosp.*, vol. 31, no. 1, pp. 307–312, 2015.

[120] B. Gordon, S. Chen, and J. L. Durstine, “The effects of exercise training on the traditional lipid profile and beyond,” *Curr. Sports Med. Rep.*, vol. 13, no. 4, pp. 253–259, 2014.

[121] U. Dal, A. T. Erdogan, A. Cureoglu, and H. Beydagi, “Resting energy expenditure in normal-weight and overweight/obese subjects was similar despite elevated sympathovagal balance,” *Obes. Facts*, vol. 5, no. 5, pp. 776–783, 2012.

[122] F. Damas, S. Phillips, F. C. Vechin, and C. Ugrinowitsch, “A Review of Resistance Training-Induced Changes in Skeletal Muscle Protein Synthesis and Their Contribution to Hypertrophy,” *Sport. Med.*, vol. 45, no. 6, pp. 801–807, 2015.

[123] J. Yan *et al.*, “Effect of 12-Month Resistance Training on Changes in Abdominal Adipose Tissue and Metabolic Variables in Patients with Prediabetes: A Randomized Controlled Trial,” *J. Diabetes Res.*, vol. 2019, pp. 1–11, 2019.

[124] L. R. Pedersen *et al.*, “Effects of 1 year of exercise training versus combined exercise training and weight loss on body composition, low-grade inflammation and lipids in overweight patients with coronary artery disease: a randomized trial,” *Cardiovasc. Diabetol.*, vol. 18, no. 1, pp. 1–13, 2019.

[125] C. A. Vella and M. A. Allison, “inflammation : The Multi-Ethnic Study of Atherosclerosis,” vol. 12, no. 6, pp. 534–540, 2019.

[126] A. S. Alberga *et al.*, “Does exercise training affect resting metabolic rate in adolescents with obesity ?,” *Appl. Physiol. Nutr. Metab*, vol. 8, no. August, pp. 1–8, 2016.

[127] T. Miller, S. Mull, A. A. Aragon, J. Krieger, and B. Jon, “Resistance training combined with diet decreases body fat while preserving lean mass independent of resting metabolic rate: A randomized trial,” *Int. J. Sport Nutr. Exerc. Metab.*, 2017.

[128] G. A. Cardoso, J. M. Salgado, M. D. C. Cesar, and C. M. Donado-Pestana, “The effects of green tea consumption and resistance training on body composition and resting metabolic rate in overweight or obese women,” *J. Med. Food*, vol. 16, no. 2, pp. 120–127, 2013.

[129] J. H. Wilmore *et al.*, “Alterations in body weight and composition consequent to 20 wk of endurance training: The HERITAGE Family Study,” *Am. J. Clin. Nutr.*, vol. 70, no. 3, pp. 346–352, 1999.

[130] C. Maffeis *et al.*, “Fluid intake and hydration status in obese vs normal weight children,” *Eur. J. Clin. Nutr.*, vol. 70, no. 5, pp. 560–565, 2016.

[131] A. S. Ribeiro, A. Avelar, B. J. Schoenfeld, R. M. Ritti Dias, L. R. Altimari, and E. S. Cyrino, “Resistance training promotes increase in intracellular hydration in men and women,” *Eur. J. Sport Sci.*, vol. 14, no. 6, pp. 578–585, 2014.

[132] J. Wärnberg and A. Marcos, “Low-grade inflammation and the metabolic syndrome in children and adolescents,” *Curr. Opin. Lipidol.*, vol. 19, no. 1, pp. 11–15, 2008.

[133] G. L. Kim *et al.*, “The association of body fat and arterial stiffness using the brachial-ankle pulse wave velocity,” *Korean J. Fam. Med.*, vol. 39, no. 6, pp. 347–354, 2018.

[134] X. Pi-Sunyer, “Changes in body composition and metabolic disease risk,” *Eur. J. Clin. Nutr.*, vol. 73, no. 2, pp. 231–235, 2019.

APPENDIX

(PARALLER PROJECTS CONCERNING PHYSICAL ACTIVITY)

PHYSICAL ACTIVITY AND DIABETES TYPE I

ISPAD Congress 2019 (ORAL PRESENTATION) – Article under submission-

Comparison of basal insulin in adolescents with type 1 diabetes during a school camp. The GLiDE Study

Tinti D, Bonfanti R, Abate Daga F, Cavallo A, Cravero D, Gollin M, Trada M, De Donno V, Bracciolini G, Mossetto C., Giorda S, Arlotto S, Porta G, Maresca M, Giraudo I, Rigamonti A, Rabbone I.

Objectives: It is not clear whether specific basal insulin gives different glycemic profiles in type 1 diabetes (T1D) adolescents regularly exercising. We conducted a study (GLiDE Study) to compare Glargine (GL) and Degludec (DE) insulin and to evaluate the percentage of time in range 70-180 mg/dl (TIR), below range (TBR) and above range (TAR) in T1D adolescents during a sport-school camp. **Methods**: 27 moderate active adolescents with T1D for at least 1 year, using either GL or DE, without co-morbidities (such as celiac or hypothyroidism), were selected to participate in a 4-day sport-school camp with different sessions of exercise.

Before camp, patients underwent physical activity tolerance test (using Bruce protocol) to evaluate maximum heart rate and aerobic fitness. Patients' clinical data and fitness levels are represented in the Table. During camp, patients reduced both basal insulins by the same amount (20%). They wore a glucose sensor (Dexcom ® G6) to be constantly, remotely monitored to prevent hypoglycemia (glucose < 70 mg/dL). All corrections were decided upon glucose value adjusted for the trend. Data were compared with values obtained 3 days before the camp. All patients also wore a Bluetooth heart rate sensor (Polar ® H10) to monitor heart rate while exercising. **Results**. We present preliminary data. No severe hypoglycemia nor diabetic ketoacidosis were observed during the camp. Mean TBR before camp was 2.8% in GL and 2.4% in DE, while during camp TBR was 0.6% and 1.6% (p=0.79), respectively. TIR before camp was 66% for GL and 51.3% for DE, while during camp it was 53.2% and 55.9% (p=0.75). TAR before camp was 31.6% for GL and 46.2% for DE, while during camp was 46.1% and 42.6% (p=0.68). Glucose consumption was comparable between groups, both during and after physical activity (p-values > 0.5) and during the night (p-values > 0.9). **Conclusions**: data show an equivalence in TBR, TIR and TAR using two basal insulins during a physical structured sport-school camp.

ISPAD Congress 2019 (POSTER SESSION) – Article under submission-

Using trend arrow-protocol in adolescents with type 1 diabetes in continuous glucose monitoring minimizes the risk of hypoglycemia during a sport-school camp.

Tinti D, Bonfanti R, Abate Daga F, Cavallo A, Cravero D, Gollin M, Trada M, De Donno V, Bracciolini G, Mossetto C., Giorda S, Arlotto S, Porta G, Maresca M, Giraudo I, Rigamonti A, Rabbone I.

Introduction: Insulin therapy needs to be adapted in adolescents with type 1 diabetes (T1D) while exercising. Hypoglycemia is the major issue and while insulin reduction is recommended, carbohydrate supplementation is also frequently needed. We conducted a study to evaluate carbohydrate supplementation to prevent hypoglycemia in T1D adolescents during a sport-school camp. **Methods**: 27 adolescents with T1D for at least 1 year, treated with multiple daily injections, without co-morbidities (such as celiac or hypothyroidism), were enrolled in a 4-day sport-school camp with different session of physical activity. During camp, participants reduced their basal insulin by 20% and pre-meal insulins up to 50%, as recommended by international guidelines. Patients wore a glucose sensor (Dexcom ® G6) to monitor directly and remotely their glucose in order to prevent hypoglycemia (< 70 mg/dL). All corrections, made with liquid glucose, were decided using glucose value corrected for the trend, with a protocol showed in the Figure. Time spent in range 70-180 mg/dL (TIR), below range (TBR), above range (TAR) and coefficient of variation (CV) were compared with values obtained 3 days before the camp. **Results**. We present preliminary data. No severe hypoglycemia and diabetic ketoacidosis were observed during the camp. Mean glucose and standard deviation resulted similar during and before the camp (177±56 and 170±59 mg/dL, p=0.38). TBR was lower during camp (1% vs. 2,7%, p=0,04), and time spent with glucose < 54 mg/dL was 0.03% (before was 0.9%, p=0.008). TIR was comparable (54.3 vs. 59.8%, p=0.25), as well as TAR (44.8 and 37.5%, p=0.14) and CV (34.6 vs. 32.2, p = 0.18). Sensor usage was above 90% both during and before the camp. **Conclusions**: correction with glucose using sensor value adjusted for trend were helpful in strongly reducing values below 70 and 54 mg/dL, without increasing TAR in T1D adolescents while exercising.

SISMES Congress 2017 (ORAL PRESENTATION)

Prevention and Perfomance in Soccer: differences between kicking and supporting lmb in soccer school children

Federico Abate Daga Luca Beratto, Ruben Allois, Matteo Ponzano, Marco Alessandria, Massimiliano Gollin

Backgroung: Physical features assessment is considered a necessary process to set appropriate training schedules for young players and to prevent injuries. Hamstring damages are one of the most common injuries in football. For this reason, coaching staff are always applying to find new ways to warn this kind of muscle injury. **Aim:** Considering this, the aim of this study consists in identify and set a preventive screening protocol comparing kicking versus supporting limb parameters in a group of children playing football. **Methods:** 20 children (8 ± 2 years, 31 ± 9 kg, 132 ± 10 cm), belonging to a local soccer school were recruited for this study. All their parents approved the attendance at this study by signing an informed consent. Children were tested using Gwalk (BTS S.p.A., Italy) to analyse the gait cycle while baropdometry and stabilometry were investigated using P-Walk balance board (BTS S.p.A., Italy). In addition, the Spinal Mouse® (Idiag, Volketswil, Switzerland) and a digital goniometer (GetMyRom for Iphone 5s, USA) were used to evaluate respectively the spine morphology and the hip joint mobility. **Results:** Results show a significant difference in the evaluation of hip joint mobility between kicking and supporting limb ($p<0.05$, 5%), while other trials did not show any significant difference. **Discussion and Conclusion:** Data shows that playing soccer can enhance joint mobility differences between the kincking and supporting limbs since childhood. Considering that mobility and strenght discrepancy between the limbs increase the risk of muscolar injuries (Knapik et al 1991) it is reccomended to propose training programs aible to minimize joint mobility differences between legs. **References** 1) Daneshjoo A., Mokthar A., Rahnama N., Yosuf A., Effects of the 11+ and harmoknee warm up programs on physical performance measures in professional soccer players. Journal of sports science & medicine. Spt 2013; 12(3): 489-495. 2) Knapik JJ, Bauman CL, Jones BH, Harris J, Vaughan L. Preseason strength and flexibility imbalances associated with athletic injuries in female collegiate athletes. The American Journal of Sport Medicine. 1991; 18(1): 76-81.

SISMES Congress 2018 (ORAL PRESENTATION) – Article under submission-

Game-based vs open-skill mulitaleral training: effects of a 12-week program on motor skill acquisition and physical fitness development in soccer school children

Federico Abate Daga, Luca Beratto, Golfieri Matteo, Massimiliano Gollin

Purpose: The importance of motor skill acquisition, physical development and health-related fitness of children has been significantly noted. (William et al, 2008). Nowadays, sport disciplines are extremely focused in young athlete development to improve performance levels and to identify future talent (Huijgen et al. 2009). This study investigates the effects of a 12-week-game-based training on motor skills acquisition compared with a traditional open-skill multilateral schedule. **Methods:** 31 children (8 ± 1 years, 29 ± 4 kg, 134 ± 5 cm, 16 ± 2 of BMI, 2±1 Years of Practice) belonging to a professional soccer academy were recruited for this study. All their parents approved the attendance at this study by signing an informed consent. Children were randomly arranged into one of the two experimental groups, trained for 12 weeks and tested on shuttle dribble test and 10x5 shuttle test using a pair of photocells (Witty, Microgate, Bolzano, Italy). **Results:** Both Game-Based Group (G-BG) and Open-Skill Group (O-SG) improved significantly in shuttle dribble test (G-BG -19%, p=0,001; O-SG -14% p=0,0037) and shuttle run test (G-BG -6%, p=0,0021; O-SG -4% p=0,0047) No difference was found between the groups at the end of the study. **Conclusion:** Data shows that both game-based training and an open-skill multilateral schedule can provide improvements in children motor skills acquisition and fitness development. Considering this, it might be possible to advice trainers to focus on both technical and fitness abilities , to ensure a complete coordinative and physical development.

References: 1) Huijgen, BCH, Elferink-Gemser, MT, Post, WJ, Visscher C. Soccer skill development in professionals. International Journal of Sports Medicine 2009; 30: 585-591 **2)** Williams HG, Pfeiffer KA, O'Neill JR, et al. Motor skill performance and physical activity in preschool children. Obesity. 2008;16(6):1421-1426.

SISMES Congress 2019 (ORAL PRESENTATION) – Article under submission-

Age-Related Effect and physical performance in pre-pubertal football players: an exploratory study

Federico Abate Daga, Vanzina Stefano, Massimiliano Gollin

Purpose: In youth football, as in many other team sports, players are usually grouped based on their chronological age. Generally, more mature children present greater anthropometric parameters and could exhibit differences in biological maturity (Carrascosa et al. 2018). Thus, this study aims to investigate the effects of age on aerobic capacity (VO2 MAX) and the technical abilities of leading the ball in U10 and U12 male players. **Methods:** Nineteen U10 and fifteen U12 boys were recruited from a local soccer school. Aerobic capacity (VO_2max) were estimated by performing a Yo-Yo Test adapted for children (Ahler et al. 2011). Technical abilities were assessed with the shuttle dribble test (Huijgen et al. 2009). **Results:** Participants' anthropometric characteristics were as follow: under 10 group: age: 9±1year, height: 133.0 ± 7.0 cm, weight: 34.5 ± 7 kg, BMI: 18.17 ± 2,3); under 12 group (age 11 ±1 year, height 146.4 ± 8.3 cm, weight 40.2 ± 9.2 kg, BMI: 18.64 ± 3.4 of BMI). U12 group showed significant differences in both technical abilities (p < 0.0001, -15% of time required) and aerobic capacity (p= 0.0016, +9%). No significant differences were detected on BMI between both groups (p=0.9423). A moderate negative correlation was observed between technical abilities and aerobic capacity (r = -0.61, p < 0.0001) **Conclusion:** U12 show better technical abilities and greater aerobic capacity (VO2 Max). On the other hand, BMI was not different between the groups. In addition, we have observed a link between technical abilities and aerobic capacity. Thus, the findings of this study suggest paying great attention to physical conditioning in pre-pubertal age, because a good fitness can positively affect the technical expression of leading the ball. **References 1)** Carrascosa A, Yeste D, Moreno-Galdó A, Gussinyé M, Ferrández Á, Clemente M, Fernández-Cancio M. Pubertal growth of 1,453 healthy children according to age at pubertal growth spurt onset. The Barcelona longitudinal growth study. An Pediatr (Barc). 2018 Sep;89(3):144-152. **2)** Huijgen, BCH, Elferink-Gemser, MT, Post, WJ, Visscher C. Soccer skill development in professionals. International Journal of Sports Medicine 2009; 30: 585-591 **3)** T. Ahler · M. Bendiksen · P. Krustrup · N. Wedderkopp. Aerobic fitness testing in 6- to 9-year-old children: reliability and validity of a modified Yo–Yo IR1 test and the Andersen test. Eur J Appl Physiol (2012) 112:871–876

SISMES Congress 2019 (POSTER SESSION)

Age-Related Effect on strenght and agility in pre-pubertal footballers

Federico Abate Daga, Fiammetta Scarzella, Roberta Bartolomei, Luca Beratto

Purpose:

Football is a multi-directional and intermittent sport that requires high technical abilities, tactical awareness, and a high level of physical conditioning (Emmonds et al. 2019). It has been demonstrated that stronger athletes are also faster during sprint performance (McBride et al 2009). The aim of this study is to investigate the effect of age on lower limb muscle strength and agility in pre-pubertal football players. **Methods:** 56 Under 10 and 72 Under 12 players were recruited from different local soccer schools. Lower limbs muscle strength was estimated based on long jump test scores while time needed to complete the hexagon test was used to evaluate agility (Beekhuinzen et al. 2009). **Results:** Demographic and anthropometric characteristics were: age 9 ± 1 years, height 136.7 ± 6.1 cm, weight 34.9 ± 9.2 kg, BMI 18.5 ± 3.9, and age 11 ± 1 years, height 153.2 ± 9.2 cm, weight 48.6 ± 11.9 kg, BMI 20.5 ± 3.8 for U10 and U12 groups, respectively. Data shows higher values of both strength ($p < 0.0001$; +24%) and agility ($p < 0.0001$; -35%) tests in U12 group compared of U10 group. In addition, BMI and long jump scores are negatively correlated ($r = -0{,}19$, $p = 0.032$) while BMI and Hexagon tests are not significantly associated. **Conclusion:** Older and more experienced children have better strength and agility abilities. Specific training programs are needed to improve physical abilities and avoid weight gain that might lead to higher BMI values and a consequent worsening in muscle strength. **References 1)** Emmonds S, Nicholson G, Begg C, Jones B, Bissas A.. Importance of Physical Qualities for Speed and Change of Direction Ability in Elite Female SoccerPlayers. J Strength Cond Res. 2019 Jun;33(6):1669-1677. 2) Beekhuizen KS, Davis MD, Kolber MJ, Cheng MS. Test-retest reliability and minimal detectable change of the hexagon agility test. J Strength Cond Res. 2009 Oct;23(7):2167-71.