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"Risk screening and exercise interventions in pediatric prevention of atherosclerotic cardiovascular disease: Links between carotid intima-media thickness and physical fitness"

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SUMMARY

The following thesis consists of 7 chapters. Chapter 1 describes the origins of atherosclerotic cardiovascular disease. In Chapter 2 the emphasis lies on the intima-media thickness of the A. carotis communis (IMT), a non-invasive diagnostic marker to determine the individual atherosclerotic cardiovascular disease risk. The validity and feasibility of the sonography are investigated and age- and sex-specific IMT norm values for a healthy pediatric population are calculated. Further possible relations between IMT and traditional cardiovascular risk factors are assessed. Chapter 3 focuses on the antiatherosclerotic effect of exercise in adults, adolescence and childhood. In Chapter 4 the cardiovascular and physical fitness status of overweight and obese children and adolescents are examined and compared to results of normal weight peers. Multidisciplinary intervention strategies of hospitalized obesity programs are evaluated and their effects on arterial structure, cardiovascular risk factors and physical fitness in obese adolescents are investigated in Chapter 5. Continuing intervention strategies towards the prevention of obesity in school settings, an existing health initiative is evaluated, regarding its positive effects on arterial structure (IMT), cardiovascular risk factors and physical fitness in young school children. Finally in Chapter 7, future considerations towards non-invasive cardiovascular risk screening, possible new risk factors and new strategies promoting physical activity and fitness are presented.

The Chapters 2 to 6 are written in a format for publication, whereas each chapter investigates its own research question and is therefore divided into Introduction and Objectives, Methods, Results, Discussions and Conclusions.

Chapter 1: Origins of cardiovascular disease

Chapter 1 introduces into the problems of atherosclerotic cardiovascular disease in children and adolescents. It describes the pathology of atherosclerosis, its origins and cardiovascular risk factors.

Chapter 2: Non-invasive diagnostic approaches in cardiovascular risk screening

Introduction and Objectives: In pediatric cardiovascular health prevention non-invasive diagnostics of subclinical atherosclerosis is essential for screenings and in-

terventional purposes. Increased IMT has been reported in the presence of cardiovascular risk factors in childhood. However, little information exists regarding the age and sex distribution of IMT as stated in adults. This study investigates first, if IMT sonography is reliable and feasible; second, calculates sex and age-specific percentiles; third, re-confirms IMT associations to cardiovascular risk parameters and analyses predictors for age-adjusted IMT.

Methods: 267 healthy pupils (age 6-17 years) were examined prospectively. Standardized IMT sonography and offline analysis were performed. Anthropometric data, BMI, body composition, blood pressure were taken; Spearman's rank correlation coefficient and multiple stepwise linear regression analyses were calculated.

Results: Intra-observer variability: Coefficient of variation was 2.42% (n=132; MD=0.012mm; r=0.849); inter-observer variability: Coefficient of variation was 1.71% (n=75; MD=0.013mm; r=0.780). Age and sex-specific IMT percentiles for age groups 8/9 to 14/15 years were calculated. IMT values were higher in boys than in girls at the same age. Systolic blood pressure and IMT were positively related in boys ($p<0.001$, $r=0.31$) and girls ($p=0.005$, $r=0.24$). Predictors for age-adjusted IMT: Systolic blood pressure was shown to be a predictor ($r^2=0.10$, ß=0.31, p<0,001) in boys; weight emerged as a predictor ($r^2=0.19$, ß=0.43, $p<0.001$) in girls.

Conclusions: The main study benefit is the provision of IMT percentiles for both sexes for the age groups 8/9 to 14/15 years. The results suggest that sex-specific prevention should be given further attention in a comprehensive and multi-risk parameters approach.

This part of the study (Chapter 2.2) is published:

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Chapter 3 Arterial function, atherosclerotic process and exercise

Introduction and objectives: Knowledge is presented from studies in adults with the focus on the antiatherosclerotic effect of exercise in adults. Further emphasis is on arterial structure, physical activity and exercise in children and adolescents. Work in healthy young children is still rare and provided contradictory findings[1-3]. There are

currently no studies that assessed relationships between physical fitness and vascular structure in young healthy children. The main objective was, to investigate relationships between health-related fitness, carotid intima-media thickness (IMT), body composition and blood pressure.

Methods**:** 197 school children, ages 6-10 years, participated. IMT, body composition, blood pressure, health-related fitness, plus hours of sports club participation were acquired.

Results: None of the children showed pathologically increased IMT. Compared to girls, boys were taller ($p=0.045$) and showed higher percentage of body fat ($p<0.001$). The IMT did not differ significantly ($p=0.109$), between boys and girls. Further no significant differences were stated about hours of sports club participation per week ($p=0.632$). Regarding health-related fitness performance, no significant differences revealed for abdominal muscular endurance strength ($p=0.086$) and cardiorespiratory endurance ($p=0.166$). Boys demonstrated significantly better upper trunk muscular endurance strength ($p=0.049$) compared to girls. Girls demonstrated significantly better harmstring, gluteal and lower back musculature flexibility ($p < 0.001$)

No significant relationships were apparent between IMT and health-related fitness.

In girls only, IMT was related to weight: $r=0.275$, $p=0.011$; BMI: $r=0.249$, $p=0.022$; body fat: $r=0.338$, $p=0.002$); the total percentage of body fat emerged as a predictor ($ß=0.364$, $p=0.003$) for IMT ($F\ [2.82] =5.415$, $p=0.006$) adjusted R square = 12%).

Conclusions: The principle findings of this cross-sectional examination of the relationship between risk factors, particularly health-related fitness, with carotid IMT in healthy, generally non-obese, young children was firstly, health-related fitness was not related to IMT. Secondly, in girls only, the analysis of IMT and anthropometric data resulted in significant relationships between IMT and body composition, namely weight, BMI and the total percentage of body fat. Additionally in girls, the total percentage of body fat was shown to be the only significant predictor variable for IMT.

Chapter 4: Early atherosclerotic wall changes in overweight and obese children: the role of physical fitness

Introduction and objectives: Studies in adults with atherosclerotic cardiovascular diseases have described structural changes of IMT in the context of obesity, such as increased IMT and greater stiffness[4]. The present study aimed to assess the vascular status (IMT) and health-related as well as skill-related physical fitness in overweight and obese adolescents compared to normal weight adolescents. Secondly, associations between traditional cardiovascular risk factors, IMT and physical fitness components in overweight and obese adolescents are analyzed.

Methods: A total of 212 children were examined. Thereof 123 children attended a hospitalized multidisciplinary intervention at the Clinic in Gaissach, Bad Tölz/ Germany and were consecutively examined in the first week after admission. The control group consisted of age-matched adolescents from Munich secondary schools and was examined by the same medical doctors and sport scientists.

The assessment included sonography of the A. carotis communis, distal of the carotid artery bifurcation on a segment ≥ 1 cm length (GE Loqiq Book XP. 10 Mhz linear probe). Further anthropometric data height, weight, BMI, body composition (FUTREX 6100 AL) and resting (15 min.) blood pressure were taken. Both sonography and anthropometric data collection were performed as previously described by Böhm and colleagues[5]. The health- and skill-related fitness test battery assessed the following components: speed of limb movement, reactive strength, speed and running coordination run, reaction and coordination, harmstring and lower back muscle flexibility, cardiorespiratory endurance, upper-trunk muscular endurance strength, and abdominal muscular endurance strength.

Results: Carotid IMT in overweight and obese adolescents was significantly ($p=0.023$) increased (0.584 ± 0.045 mm) compared to healthy controls (0.532 ± 0.045 mm). There was still evidence of statistical differences after adjustment for sex, age, height and diastolic blood pressure. This study provides further documentation of associations between IMT and age ($r=0.213$, $p=0.041$), weight ($r=0.225$, $p=0.032$), BMI ($r=0.263$, $p=0.015$) in overweight and obese children. In the multiple linear regression analysis BMI was shown to be the only predictor for variable (ß=0.263, $p=0.030$) for IMT (F [1.66] = 4.899, $p=0.030$), adjusted R^2 = 5.5%. However, after IMT was adjusted for sex and age the statistical significance reduced to a level that did not reach the formal level of significance (r=0.185, p=0.065).

Health-related and skill-related physical fitness in overweight and obese adolescents was impaired in all tested components. Associations between physical fitness and traditional cardiovascular risk factors could be stated, but no correlations of physical fitness components and IMT could be assessed.

Conclusion: The study underlines that vascular structure changes with increased body weight. It could be proven that increased IMT is present in overweight and obese children. Further overweight and obese children demonstrated reduced health- and skill-related physical fitness in almost all test components. The results emphasize the need off an early focus on skill-related fitness. Better motor skills might have the effect to encourage obese children to more activity and exercise. Although a correlation between IMT and physical fitness could not be approved, physical fitness was correlated to cardiovascular risk factors. The awareness of these associations in combination with the fact that obesity in adolescents is an important risk factor for cardiovascular disease and mortality in later life, highlights the importance of early interdisciplinary prevention measures including motivation to more activity and early medical and fitness screening for possible individual risk factors.

Chapter 5 Intervention strategies in obese children and adolescents: the importance of exercise

Introduction and objectives: Little is known about the impact of interventions on the overt or subclinical incidences of vascular structure changes in a pediatric population. Therefore in the present part of the study aimed to assess, if a short-term stationary rehabilitation program has an effect on cardiovascular risk factors, including vascular structural changes and health-related as well as skill-related physical fitness components. It was hypothesized that a 4-week hospitalized multidisciplinary intervention reduced cardiovascular risk factors such as BMI, the total percentage of body fat, systolic and diastolic blood pressure, resting heart rate and IMT. Further it was assumed that by the intervention health-related and skill-related physical fitness improved resulting in better strengths, speed, coordination, endurance capacity and flexibility.

Methods: 85 obese children and adolescents (age 11-15 years) who attended a hospitalized intervention at the Rehabilitation Center, Clinic Gaissach, Bad Tölz/Germany were consecutively examined at baseline and 4-weeks later. The intervention program was multidisciplinary and based on daily physical exercise, nutrition and behavior therapy. The medical examination including anthropometric data collection and sonography of carotid IMT was conducted as previously described by Böhm and colleagues[5]. The health- and skill-related fitness test battery assessed the following components: speed of limb movement, reactive strength, speed and running coordination run, reaction and coordination, harmstring and lower back muscle flexibility, cardiorespiratory endurance, upper-trunk muscular endurance strength, and abdominal muscular endurance strength.

Results: Anthropometric measurements revealed significant decreases in weight, BMI, and body fat mass (all $p<0.001$). The intervention produced a significant decrease in systolic blood pressure ($p<0.001$) and diastolic blood pressure ($p=0.037$). Further the heart rate decreased significantly ($p<0.001$). After 4 weeks the IMT did not change significantly ($p=0.440$). Results in physical fitness demonstrate in most tests an increase in performance: the tapping frequency significantly improved ($p<0.001$); the ground contact time assessed by drop jumps reduced significantly ($p<0.011$). The complex reaction test revealed a significant better overall coordination, resulting in a faster reaction time (<0.001); increase performance was assessed in cardiorespiratory endurance ($p<0.001$) and in harmstring, gluteal and lower back muscle flexibility ($p=0.048$). The running coordination and speed ($p=0.121$), the upper trunk ($p=0.519$) as well as the abdominal muscular strength and endurance (0.781) did not change after 4 weeks hospitalized intervention.

Conclusions: In advantage to invasive diagnostics the ultrasound measurement can demonstrate the effect of the intervention program clearly on the level of the vascular system, since it enables an insight to the health of the blood vessel. However, pathological changes need longer time to be reduced.

The multidisciplinary intervention with a focus on daily physical activity and sport revealed an enhancement in speed of lower limbs, reactive strength, complex coordination and reaction time, flexibility and endurance capacity. These positive effects might be beneficial for long-term physical activity and sport motor skill improvement.

Publication

Böhm B, Hartmann K, Kallweit C, Bauer, CP, Oberhoffer R: Retro- and prospective analysis of cardiovascular risk factors in rehabilitative intervention programs for obese children. 43rd Annual Meeting - association for European Paediatric Cardiology and 18th Spring meeting - European Heart Surgeons Association 21 - 24. Mai 2008 in Venedig. Cardiology in the Young 2008, 18, Suppl. 1 43-44.

Chapter 6 Obesity prevention in school settings

Introduction and objectives: The Bavarian Ministry of Environment and Public Health launched a health initiative "Gesund. Leben. Bayern". In this health promotion campaign, the physical activity program "Sport passed 1 o'clock" affiliates regional sport clubs and schools for better networking and combines resources with the main aim to increase children's physical activity and integration to sports clubs. The main aim of this pilot study was to determine the effect of school basketball training, without a dietary intervention, on body composition, health- and skill-related physical fitness and non-invasive cardiovascular risk factors.

Methods: Sixty-four children could be integrated in the analysis, comparing baseline and post examination. Anthropometric data collection and sonography of carotid IMT was performed as reported by Böhm and colleagues[5]. In the health- and skill-related physical fitness test a multitude of fitness components were tested, including cardiorespiratory endurance, muscular strength, muscular endurance strength, speed, coordination, reaction time and flexibility. The intervention consisted of 90 minutes basketball training per week, for a period of 6 months. The training was organized and conducted by a nationally certified basketball coach of the SV Germering.

Results: The children of the intervention group revealed no difference in BMI ($p=0.093$); the total percentage of body fat significantly increased ($p=0.011$); the systolic blood pressure significantly increased ($p=0.013$); diastolic blood pressure ($p=0.124$) as well as resting heart rate ($p=0.644$) and IMT ($p=0.877$) did not change significantly by the intervention.

In the control group no significant differences could be assessed in BMI ($p=0.056$); the total percentage of body fat significantly increased ($p<0.001$); no changes in systolic ($p=0.430$) and diastolic blood pressure ($p=0.215$) revealed; resting heart rate was significantly reduced ($p=0.006$); however, IMT significantly increased ($p=0.045$).

Both, children of the intervention and the control group, significantly improved their health-and skill-related physical fitness: abdominal muscular endurance (both $p<0,001$); speed of limb movements (both $p<0.001$), running speed and coordination (both $p<0.01$) as well as in simple coordination ($p=0.003$ in the intervention group, $p=0.043$ in the control group) and complex coordination (both $p<0.001$).

Conclusions: The "Sport past 1 o'clock program" of the Bavarian Ministry of Environment and Public Health demonstrated a successful network between community policies and programs with sports clubs and schools. The results showed a significant improvement of vascular structure in children of the intervention group, but could not further reveal significant effects on traditional cardiovascular risk factors. The intervention program further improved mainly basketball-related and trained skills such as tapping, reactive strength, flexibility and abdominal strengths. However, the children of the control group also increased their performance. Thus, the effect of the intervention program is not explicitly a result of the additional training. Moreover, it demonstrated an effect of normal maturation over 6 months. Furthermore the results underline that one bound of additional exercise in not enough for a significant improvement in fitness in relation to the control group.

Chapter 7 Future considerations

Future considerations, regarding non-invasive cardiovascular risk screening in pediatrics, linking arterial structure and function with physical fitness, exercise and physical activity, the clinical relevance are described.

Annotation

The pilot study "cardiovascular risk screening in primary school children" (Chapter 6) was awarded with the "Bayrischer Gesundheitsförderungs- und Präventionspreis 2006". The Landeszentrale für Gesundheit in Bayern e.V. gave credit for the successful cardiovascular prevention intervention program in a school setting (15.11.2006).

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Ethics approval (1162/04)

The Ethics Committee of the Faculty of Medicine of the Technische Universität München approved all included study protocols of the thesis. Written informed consensus was given by all the participants and their legal representatives.

1 Origins of atherosclerotic cardiovascular disease

1.1 Pathology of atherosclerosis in youth and the cardiovascular risk factors

Atherosclerosis, the arterial lesion underlying most forms of adult cardiovascular disease, was formerly considered an inevitable consequence of aging. The natural history of atherosclerosis was described by Strong and colleagues (1962)[6] and Strong and McGill (1963)[7]. The earliest morphological change clearly identified as atherosclerosis, is the „fatty streak“, an accumulation of lipid-filled macrophages („foam cells“) in the intima of large muscular and elastic arteries. The predominant lipids are cholesterol and its esters. With age liquid constitutes to accumulate in magrophages adjacent smooth cells and extracellular spaces. Smooth cells and connective tissue proliferate to encapsulate the lipid and form the „fibrous plaque“. Vascularization may lead to hemorrage within the plaque, resulting in rapid swelling and arterial occlusion. Calzification may stabilize the plaque. The resulting clinical syndrome depends on the location of the affected artery. Detailed characteristics of these stages of progression of atherosclerosis have been thoroughly described and illustrated in publications of the Committee on Vascular Lesions of the Council on Atherosclerosis.[8,9]

Factors that thought to be involved in the development of atherosclerotic vascular lesion may be grouped under several headlines: the anatomic, hemodynamic, hematologic, intrinsic, metabolic, inflammatory and reparative and temporal factors. The complexity of the development was early stated by McMillan in 1973[10]: *“there is no exclusive or unique early lesion for all atherosclerosis but a variety of initial changes such as endothelial injury, platelet adhesion, altered endothelial permeability with insudation of blood proteins, infilteration of lipoproteins, and the like which can lead to injury-repair reactions and in some circumstances to plaque building. Such initial events can be episodic, repeated, evanescent, cumulative and synergistic. They are not conceived to be confined to one period of life and indeed one very often finds lesions like those of childhood among more advances lesions of arteries from adults”.*

This description illustrates the variety of interacting influences that occur over lifetime in the genesis of atherosclerotic lesions, beginning at birth.

More recent research on the atherosclerosis focused on the aspect of inflammation[11]. The role of inflammation in the development of atherosclerosis has been appreciated in the past decade and subsequent processes leading to increased cellular oxidation have been implicated[11,12]. Atherosclerosis, the main cause of coronary artery disease is now thought to be a chronic inflammatory disease in which immune mechanisms interact with metabolic risk factors to initiate, maintain and activate arterial lesions[13].

The focus is on the functional health of the vascular endothelium, where the atherosclerotic process starts. The vascular endothelium is a highly active tissue with multiple functions, particularly that of regulating vessel tone and of the control of blood flow[14]. The endothelial products, most important nitric oxide (NO), generated by wall shear stress, protect the vessel wall from inflammation and proliferation of smooth muscle cells and prevent the adhesion of plaques. When the endothelium becomes dysfunctional, NO is reduced. The endothelium itself then attracts inflammatory cells and serves as a nidus for pallet and cell aggregation – the beginning of the atherosclerotic process. There are various cardiovascular risk factors for endothelium dysfunction described in the literature. Those are LDL cholesterol, hypertension and smoking, the aging process, diabetes mellitus and hyperglycaemia, obesity and physical inactivity[15].

1.2 Introduction to pediatric atherosclerosis prevention

Since the atherosclerotic progression covers a long phase before the development of measurable plaques are manifested, it is important to evaluate the arterial health status of children and adolescents, for individual risk assessment. Additionally it is important to analyze cardiovascular risk factors that are responsible for and in relation with the atherosclerotic progression[16]. Cardiovascular risk factors act early in life and have a major impact on the development of atherosclerosis[17].

One of the early and most significant American multicenter study, organized by fifteen cooperating centers, to determine pathobiological aspects of atherosclerosis in youth was the PDAY-Study, Pathobiological Determinants of Atherosclerosis in Youth[18]. Detailed descriptions of methods and results have been presented in a number of publications[19-25]. Summarizing the implications of the results from the pathologic studies it can be stated that atherosclerosis begins in childhood – atherosclerotic lesions are present in almost all aortas and about half of the right coronary arteries by the late teen (10-15 years old) and increase in extent and severity through the early thirties. Second, risk factors, such as male sex, cholesterol, smoking, hypertension, obesity, hyperglycemia, accelerate the progression in youth; third, there is potential for primary prevention and intervention should begin early – the rapid increase in raised lesions at about the age 25 years suggest that risk factor control should be initiated prior to that age.

These conclusions from the PDAY study are consistent with the observation that serum cholesterol levels in young adults predict coronary heart disease risk at middle age[26]. Also van Horn and Greenland[27] stated that prevention of coronary artery disease is, indeed a pediatric problem.

The Bogalusa Heart Study underlines that early manifestation of atherosclerosis is manifested to traditional risk factors[28]. The study is one of the longest and very detailed prospective studies of children with a focus on the early natural history of coronary artery disease. The study began in Bogalusa in 1973 and is still ongoing. More than 16 000 individuals (school-aged children and young adults up to 35 years of age) have participated, and more than 9500 have had multiple measurement of cardiovascular risk factors, including BMI, triceps skinfold thickness, lipid profile and smoking status. The observations from the Bogalusa Heart Study have shown that etiologies of adult CVD, atherosclerosis, coronary artery disease, and essential hypertension begin in childhood, with early documented anatomic changes as early as 5 to 8 years. Further a "tracking" of risk factors into adulthood has been described[29]. Furthermore traditional risk factors that are present in childhood predict cardiovascular risk in adulthood[28,30,31].

2 Non-invasive diagnostic approaches in pediatric cardiovascular health prevention - the visualization of the artery, its structure and function

In the last years, technological advancement made it possible to underline the screening of risk factors non-invasively mostly by ultrasound measurements. Several non-invasive and relatively easy to obtain measures of arterial structure and function have shown to be clinically useful in pediatric screenings and diagnostics, getting an "inside view" of arterial health.

The blood vessel consists of tree concentric layers: intima, media and adventitia. The intima, adjacent to the blood vessel lumen, is composed of a monolayer of endothelial cells with underlying tissue. The endothelial cells perform important roles in regulating vascular tone and structure[32]. These roles include, providing a non-thrombotic surface, maintaining vascular tone by releasing small molecules such as nitric oxide, prostacycline and endothelin (which moderate vasodilatation and vasoconstriction) and further providing a non-adherent surface of leucocytes[33].

The arterial structure and function is measured non-invasively, using high-resolution ultrasound. Those measurements are primarily the measurement of carotid intima-media thickness (IMT) of the A. carotis communis, diagnosing anatomic changes, endothelial function (physiologic changes) (conduit-artery endothelial function), by assessing the flow-mediated dilatation (FMD) of the brachial artery[16,34,35] and arterial compliance e.g. arterial stiffness (mechanical changes) on the carotid artery, aorta or brachial artery, measuring the change in vessel diameter between systole and diastole or pulse wave velocity (PWV). PWV is a measure of the speed of the arterial pressure wave propagation and is an inverse index of arterial wall stiffness[36,37].

Those new non-invasive diagnostic methods that are applicable in children are "attractive" in the pediatric age group to prevent, detect and ameliorate conditions in childhood that lead to atherosclerotic cardiovascular disease later in life[38].

2.1 The IMT – a non-invasive measure of arterial structure

In non-invasive diagnostics of atherosclerotic progression the intima-media thickness (IMT) is measured to quantify the atherosclerotic wall process and serves as a subclinical marker of atherosclerosis and further is a strong marker of cardiovascular disease burden.

The IMT can be used to predict myocardial infarction and stroke[39]. It has been further indicated in adults that an increased IMT is associated with an increased risk of myocardial infarction and stroke, even without a previous history of cardiovascular disease[40]. IMT can be viewed as a descriptive index of individual atherosclerosis in adults[41].

2.2 Sex differences of carotid intima-media thickness in healthy children and adolescents

The aim was to determine norm values for IMT in a pediatric population and to investigate the validity and feasibility of the sonography of the carotid IMT. Therefore the following study was conducted and published.

Due to the authors' rights and responsibilities of the Elsevier journal "Atherosclerosis", the paper is integrated as full-text in this dissertation.

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Sex differences of carotid intima-media thickness in healthy children and adolescents

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ABSTRACT

Objectives: In pediatric cardiovascular health prevention non-invasive diagnostics of subclinical atherosclerosis is essential for screenings and interventional purposes. Increased carotid artery intima-media thickness (IMT) has been reported in the presence of cardiovascular risk factors in childhood. However, little information exists regarding the age and sex distribution of IMT as stated in adults.

This study investigates first, if IMT sonography is reliable and feasible; second, calculates sex- and age-specific percentiles; third, re-confirms IMT associations to cardiovascular risk parameters and analyses predictors for age-adjusted IMT.

Methods: 267 healthy pupils (age 6–17 years) were examined prospectively. Standardized IMT sonography and offline analysis were performed. Anthropometric data, BMI, body composition, blood pressure were taken; Spearman's rank correlation coefficient and multiple stepwise linear regression analyses were calculated.

Results: Intra-observer variability: CV was 2.42% ($n = 132$; MD = 0.012 mm; $r = 0.849$); inter-observer variability: CV was 1.71% ($n = 75$; MD = 0.013 mm; $r = 0.780$). Age- and sex-specific IMT percentiles for age groups 8/9 to 14/15 years were calculated. IMT values were higher in boys than in girls at the same age. Systolic blood pressure and IMT were positively related in boys ($p < 0.001$, $r = 0.31$) and girls ($p = 0.005$, $r = 0.24$). Predictors for age-adjusted IMT: systolic blood pressure was shown to be a predictor ($r^2 = 0.10$, $\beta = 0.31$, $p < 0.001$) in boys; weight emerged as a predictor ($r^2 = 0.19$, $\beta = 0.43$, $p < 0.001$) in girls.

Conclusion: The main study benefit is the provision of IMT percentiles for both sexes for the age groups 8/9 to 14/15 years. The results suggest that sex-specific prevention should be given further attention in a comprehensive and multi-risk parameters approach.

1. Introduction

In pediatric cardiovascular health prevention non-invasive diagnostics are of utmost importance for screenings and interventional purposes. Cardiovascular risk factors in childhood, such as obesity and hypertension [1–3] are the key issues for the development of subclinical cardiovascular disease [4].

The thickness of carotid artery intima-media (IMT) is an excellent surrogate marker of cardiovascular risk, used in stroke units and adult cardiology for non-invasive monitoring of the effect of therapeutic strategies [1,5]. Several studies described increased IMT in children with known cardiovascular risk [6–8] and a "tracking" of those factors into adulthood [9]. The Cardiovascular Risk in Young Finns Study underlines hypertension as a major contributor to atherosclerosis emphasizing sex differences in predicting endothelial dysfunction [10].

In contrast to adulthood [11,12], only little information exists regarding the age distribution of IMT in a healthy pediatric population, despite the need of early cardiovascular prevention.

A Japanese study [13] investigated the relationships between IMT and age in childhood analysing 60 healthy children (5–14 year) and described a linear increase of mean IMT with age. Sex differences of IMT as well as sex-specific percentiles, useful for follow-up studies, are not yet reported for a European pediatric cohort. Previous studies examined carotid IMT in a healthy population have generated conflicting results [14,15], possibly due to methodological aspects.

Reference values of IMT in healthy German adults were described by others [16] who underlined higher IMT values for men in comparison to women for the age group 40–54 years. The present study emphasizes the determination of IMT percentiles in German children under strictly standardized sonographic condi-

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tions and analysis, using newest technologies. Knowing that sex differences exist in adults [16] and that IMT is associated with age [13], the objectives of this study were to investigate the following hypotheses: (i) the sonographic measurement is reliable and feasible in healthy children; (ii) there are sex differences in IMT in healthy children, requiring sex- and age-specific norm values; (iii) height, weight, BMI, the total percentage of body fat and blood pressure are associated with IMT and predictors for increased IMT in healthy boys and girls.

2. Materials and methods

2.1. Subjects

267 children (143 girls and 124 boys, mean age girls 10.2 years (range 6–17 years); boys 10.8 years (range 6–17 years) from Munich schools were examined prospectively.

All legal representatives of the children provided written informed consent before examination. The study was approved by the Ethics Commission of the Technische Universität München, Germany (protocol number: 1162/04). According to personal questionnaires, all subjects were free from acute or chronic illnesses.

2.2. Anthropometry

Body weight, including only light shirts and shorts, was measured to the nearest 0.10 kg using an electronic scale (SECA 702), parallel height was measured to the nearest millimeter on bare foot using SECA 702. Body mass index (BMI) (kg/m^2) was calculated from the ratio of mass/height^2.

The percentage of body fat was measured with a body fat analyser (FUTREX 6100/XL, Germany) using patented near-infrared measurement technology [17]. The sensor was placed on the non-access upper arm for 5 s. The mean value out of two measurements was documented and used for further statistical analysis.

After 15 min rest, blood pressure was measured (Riva Rocci) twice at the right arm in a supine position (legs not crossed) using a calibrated, age-specific sphygmomanometer.

2.3. Ultrasound measurements

In a recumbent position with slightly reclined neck, the two-dimensional ultrasound examination of the right common carotid artery was performed with a 10 MHz linear transducer (Logiq Book XP, GE Germany) following a standardized protocol. The carotid tree was first scanned with the transducer positioned at the lateral side of the neck and then rotated by 90° to achieve a longitudinal image of the carotid artery. The lumen of the common carotid artery and the carotid bulb were maximized with gain settings to optimize image quality. The image included the beginning of carotid bifurcation and the common carotid artery and was focused on the posterior (far) wall. The distance between the lumen–intima interface and the media–adventitia interface reflects the intima-media complex, which was displayed horizontally over the maximal possible distance. A moving scan with a duration of 5 s was recorded and stored in digital format for offline analyses. From the 5-s clip image, three best quality end systolic-frames of each subject were selected and used for offline analyses.

IMT was measured offline according to the standardized protocol by semi-automated edge detection using a measurement computer software package (Sigma Scan Pro 5.0) previously described by Sander et al. [18]. In brief, IMT measurements were performed 8–18 mm proximal to the carotid artery bifurcation on a strictly horizontal segment. On the 1-cm segment, 11 measurements of the IMT of the far wall were automatically attempted at 1-mm increments, with the image analysis system and the IMT of the segment was estimated as the mean of these 11 measurements. This approach has been sufficiently evaluated for superficial arteries in adults [19]. From the average of three measurements in three different images a mean IMT value was determined. For the calculation of intra- and inter-observer variability measurements of 132 and 75 patients were taken, respectively. Two independent sonographers both certified and blinded to the anthropometrical data of the patients examined the participants and performed the offline analysis separately. For the analyses of the inter- and intra-observer variability the same methods were used. For the inter-observer variability the same three selected end systolic frames were analysed, respectively, three different frames of each subject for intra-observer variability.

2.4. Statistical analysis

All data were entered and analysed in SPSS 15.0 for Windows. Weight groups were determined by age- and gender-specific BMI reference values for German children as standardized by the German Obesity Association [20], defining BMI >90th percentile as overweight, >97th percentile as obese. Underweight is defined as BMI <10th percentile. Hypertension was defined with regard to sex and age by values above the 95th percentile of the International Task Force [21].

Descriptive statistics of anthropometric data, BMI, body composition, blood pressure were performed and for the calculation of age-specific IMT percentiles, 2-year age groups were assigned. The study population allowed the calculation of the 25th, 50th and 75th percentiles for both sexes from age 8/9 years to 14/15 years including confidence intervals (CIs) [22].

Means and standard deviations (SDs) for differences between observers were calculated. The inter- and intra-observer error (s) was calculated according to the formula $s = \mathrm{SD}/\sqrt{2}$. The coefficient of variation (CV) describes the difference as a percentage of the pooled mean value $\bar{x}$ and was calculated according to the formula:

$$\mathrm{CV} = \frac{s \times 100\%}{\bar{x}}$$

The non-parametric Spearman's rank correlation test was used in the correlation analysis with the relationship illustrated using Pearson's correlation coefficient (r).

Normal distribution was tested using Kolmogorov–Smirnov Test. Since the anthropometric and IMT data show a non-Gaussian distribution, data are presented as median (interquartile range) and non-parametric tests were performed. To identify differences in gender Mann–Whitney U-test was performed. Comparison between age groups was identified using a two-sided Kruskal Wallis test. Multiple stepwise linear regression analyses were performed with age-adjusted IMT as dependent variables, and BMI adjusted for age and sex, total body fat, systolic and diastolic blood pressure as independent variables for both sexes. Residuals were tested and the distribution was normal. All covariates included in the model were tested for interactions with each other. Because the variance inflation factor (VIF) was <5 and condition indices were <15 no correction for collinarity of the data was necessary [23]. A p-value of less than 0.05 was considered statistically significant.

3. Results

The characteristics of the sample population are displayed in Table 1. 11.9% of the girls were overweight and 5.6% underweight and 11.3% of the boys were overweight and 6.5% underweight. In girls, a significant increase of body fat (%) from age 10/11 to 12/13 years was illustrated (Fig. 3, supplementary appendix), whereas in boys a significant decrease of the percentage of body fat was

Table 1
Characteristics of the sample population. Values are presented as median and interquartile range (IQR) (IMT, carotid intima-media thickness). For the comparison of gender, Mann–Whitney *U*-test was calculated.

	Total (267)		Boys (*n* = 124)		Girls (*n* = 143)		*p*-Value
	Median	IOR	Median	IQR	Median	IQR	
Age (years)	10	(8–13)	10	(8.5–13)	9	(8–12)	0.061
Height (m)	1.42	(1.34–1.59)	1.45	(1.37–1.58)	1.41	(1.31–1.60)	0.028
Weight (kg)	36.7	(29.5–49.9)	37.5	(30.4–51.1)	34.4	(28.8–49.0)	0.075
BMI (kg/m^2)	17.79	(15.87–19.77)	17.9	(16.3–19.8)	17.5	(15.8–19.7)	0.337
Body fat (%)	21.1	(17.8–24.6)	22.1	(18.8–24.6)	19.7	(17.5–24.7)	0.097
Systolic blood pressure (mmHg)	110	(100–118)	110	(100–120)	110	(100–115)	0.190
Diastolic blood pressure (mmHg)	70	(63–75)	70	(60–75)	70	(65–75)	0.653
IMT (mm)	0.51	(0.48–0.56)	0.529	(0.49–0.56)	0.515	(0.47–0.55)	0.021

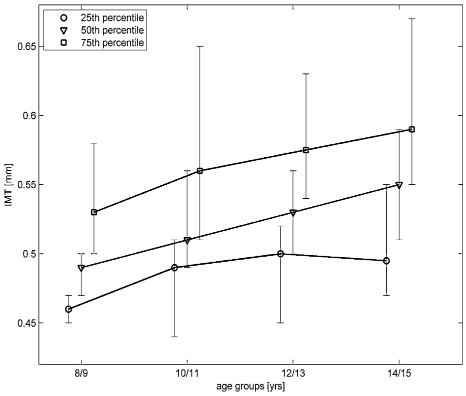

Fig. 1. Percentiles of carotid intima-media thickness (IMT) in girls according to age.

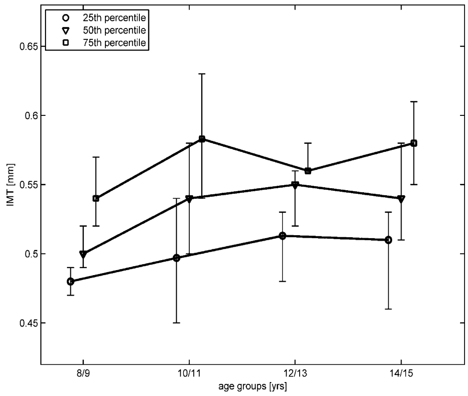

Fig. 2. Percentiles of carotid intima-media thickness (IMT) in boys according to age.

demonstrated from age group 12/13 to 14/15 years (Fig. 4, supplementary appendix). This decrease of body fat (%) correlates positively ($p < 0.001$, $r = 0.55$) with an increase in height (m) in boys.

19.6% of the girls were hypertensive (6.3% systolic, 7.7% diastolic, 5.6% systolic and diastolic hypertension), 19.4% of the boys (9.7% systolic, 6.5% diastolic and 3.2% systolic and diastolic hypertension).

In children, the IMT ultrasound examination time was approximately 5 min/patient; the offline analysis 8 min/picture. The intra-observer variability presented as the coefficient of variation (CV) was 2.42% ($n = 132$, deviation mean 0.012 mm; $r = 0.849$). The inter-observer variability described as CV was 1.71% ($n = 75$, deviation mean 0.013 mm; $r = 0.780$). No plaque was detected in any subject.

Regarding the total study population IMT increased with age. Median IMT at age 8/9 years is 0.51 mm (0.48–0.54 mm), at age 10/11 years is 0.52 mm (0.49–0.57 mm), at age 12/13 years is 0.54 mm (0.50–0.56 mm) and at age 14/15 years is 0.55 mm (0.51–0.58 mm). Age- and sex-specific IMT percentiles for age groups 8/9 to 14/15 years are presented in Figs. 1 and 2. Values are displayed in Table 2. Due to the small number of participants ($n < 16$) percentiles for age groups 6/7 and 16/17 years in boys and girls were not calculated. A mean IMT increase of 0.02 mm in 2 years could be well documented for girls until an age of 14/15 years. In boys, the mean IMT increased 0.04 mm from age 8/9 to 10/11 followed by stagnation. IMT values were significantly ($p = 0.021$) higher in boys than girls.

For both sexes, IMT and height were positively associated (boys: $p = 0.007$, $r = 0.24$; girls: $p < 0.001$, $r = 0.38$), In addition, IMT was positively associated with age in both sexes (boys: $p = 0.002$, $r = 0.28$; girls: $p < 0.001$, $r = 0.32$) and to body weight (boys: $p = 0.015$, $r = 0.22$; girls: $p < 0.001$, $r = 0.39$). In girls only, a positive relationship ($p < 0.001$) between IMT and BMI ($r = 0.35$), plus IMT and body fat ($p < 0.001$, $r = 0.41$) was found. In boys, correlations between IMT and BMI ($p = 0.11$, $r = 0.14$) as well as IMT and body fat ($p = 0.46$, $r = 0.06$), could not be approved.

Table 2
Percentile values and confidence interval (CI) of carotid intima-media thickness (IMT) in boys and girls according to age.

	Age (years)	*n*	IMT percentiles (mm)					
			25th	CI	50th	CI	75th	CI
Boys	8/9	40	0.480	0.470–0.490	0.500	0.490–0.520	0.545	0.520–0.570
Girls		62	0.460	0.450–0.470	0.490	0.470–0.500	0.530	0.500–0.580
Boys	10/11	22	0.497	0.450–0.540	0.540	0.500–0.580	0.583	0.540–0.630
Girls		19	0.490	0.440–0.510	0.510	0.490–0.560	0.560	0.510–0.650
Boys	12/13	30	0.513	0.480–0.530	0.550	0.520–0.560	0.560	0.560–0.580
Girls		25	0.500	0.450–0.520	0.530	0.500–0.560	0.575	0.540–0.630
Boys	14/15	18	0.510	0.460–0.530	0.540	0.510–0.580	0.580	0.550–0.610
Girls		17	0.495	0.470–0.550	0.550	0.510–0.590	0.590	0.550–0.670

Table 3
Multiple stepwise linear regression analysis with IMT (in millimeters, adjusted by age) as the dependent variable. BMI, total percentage of body fat, systolic and diastolic blood pressure as independent variables for both sexes.

	Boys			Girls		
	β	r^2	*p*-Value	β	r^2	*p*-Value
Height	–	–	–	–	–	–
Weight	–	–	–	0.43	0.19	<0.001
BMI	–	–	–	–	–	–
Body fat	–	–	–	–	–	–
Systolic blood pressure	0.31	0.10	<0.001	–	–	–
Diastolic blood pressure	–	–	–	–	–	–

Systolic blood pressure and IMT were positively related in boys ($p < 0.001$, $r = 0.31$) and girls ($p = 0.005$, $r = 0.24$).

In multiple linear regression analysis (Table 3) with age-adjusted IMT (in millimeters) in boys, a significant model emerged (F [1.188] = 12.83, $p < 0.0001$) adjusted $R^2 = 10\%$). Systolic blood pressure was shown to be the only significant predictor variable ($\beta = 0.31$, $p < 0.001$). In girls, weight emerged to be the only significant predictor variable ($\beta = 0.43$, $p < 0.001$) (adjusted $R^2 = 19\%$, F [1.131] = 30.17, $p < 0.001$).

4. Discussion

In consideration of the fact that IMT is an important non-invasive marker of subclinical atherosclerosis and essential for screenings and interventional purposes, it is necessary to assess IMT percentiles in a well-controlled and well-characterized study group. Currently no data exist of a defined healthy German pediatric group that assessed IMT percentiles using a strict study protocol.

Regarding the feasibility, IMT ultrasound was easy to perform and well tolerated. Reliability was good showing low inter- and intra-observer variability of less than 3%. Previous studies formulating percentiles [14] described a higher coefficient of variation of 4.9% for the intra-observer variability, whereas others [15] did not describe the reliability of the used method at all.

In general median sex-specific IMT values show differences to previous studies, possibly due to differences in the ultrasound technology and measurement techniques.

Our analyses as well as those of Woo et al. [6] and Wunsch et al. [24] were based on the far (posterior) wall intima-media complex.

Diverse ultrasound frequencies were utilized in previous studies making comparisons of IMT values complex. In the present study a linear transducer of 10 MHz was used so did Woo et al. [6] and Wiegman et al. [8], however Wunsch et al. [24] and Meyer [7] used an even higher frequency of 15 MHz and 14 MHz, respectively.

The values between the <10th percentile and the 25th percentile in the present study correspond to studies of Woo et al. [6] who examined a small number of healthy and obese boys ($n = 36$, mean age 10.3 ± 0.95 years). In their study the mean IMT of healthy boys was measured with 0.45 ± 0.04 mm. Similar IMT values of 0.47 mm (0.42–0.55 mm) were documented by Wunsch et al. [24] in 10 controls (30% male, median age 9 years).

De Groot et al. [25] mainly focused on the screening of adults. Next to this group IMT values for younger healthy controls ($n = 44$, mean age 14.9 ± 2.8 years of 0.53 ± 0.03 mm) were presented which correspond to the described values of the 50th percentile in our analyses.

The study of Meyer [7], describing lower IMT values in 30 children with a mean IMT value of 0.38 ± 0.05 mm, is methodologically problematic, since mean intima-media complex was calculated measuring near and far walls. It is well established that the clinical relevance of measurements of the near wall, which is difficult to visualize, is uncertain and that IMT can only be measured in a valid way in the far wall position [26]. Jourdan et al. [15] describes lower IMT values only used manual caliper measurements of the IMT according to the leading edge method.

Ishizu et al. [13] found a linear increase of IMT with age in 60 healthy children (27 boys, 33 girls; age range 5–14) [IMT in millimeters = (0.009 × age in years) + 0.35]. The described increase by age in a Japanese cohort corresponds to the increase that we found in boys of 0.04 mm from age 8 to 10 years. In girls, IMT increased linear with 0.02 mm in 2 years. A reason of these differences could be due to the fact that the present study took sex differences into regard as well as the Japanese e.g. German parentage.

In extension to previous studies on norm values [14,15] the present study presents sex-specific IMT values in childhood. The results of the present study showed higher values of IMT in boys than in girls. Therefore normal values of the carotid IMT in children and adolescents of both sexes from age 8 to 15 years were defined. Current studies of Osika [27] revealed that boys have a greater radial arterial intima-media thickness, compared with girls, indicating that sex differences in peripheral arteries already exist in the young. In the present study those sex differences and anthropometric changes were well assessed in the complex and variable pubertal phase.

Cross-sectional data of early pubertal girls show that higher estrogen levels are associated with a gynoid distribution of body fat [28]. This biological fact was resembled by the present results showing a significant increase of the total percentage of body fat between the ages of 10/11 to 12/13 years in girls only, as a sign of beginning puberty. The continuous and significant increase of IMT at this phase was indeed associated with the increase in total percentage of body fat. In comparison to boys IMT is reduced in girls who are at the beginning of their puberty. One contribution factor for this result could be the direct effect of estrogen. Protective effects of estrogen on the cardiovascular system are described previously which might contribute to protective effects on the arterial wall with resulting thinner intima-media thickness in girls as presented in this study [29].

From the onset of puberty in males, our results show IMT stagnation in coherence with a growth spurt resulting in an increased BMI and a strong reduction of the percentage of body fat. The increased BMI in association with IMT stagnation could explain that no correlation between IMT and BMI was detected in boys. A possible input of sex hormones could explain those sex differences which need further analysis, especially on the contribution of andogens and testosterone in reference to vascular remodeling and atherosclerosis.

The multiple linear regression analysis suggests a link between atherogenic changes and cardiovascular risk factors such as obesity and hypertension.

These findings are in keeping with previous reports in adolescents 10–20 years of age [15]. Moreover, the study demonstrated that BMI and body fat are associated with IMT in the female population and additionally that weight emerged as a predictor in girls. Similar findings have also emphasized this association in adolescents (age 10–24 years) and adults (age 35–54 years) [14] in a smaller number of patients. These data suggest that overweight of any degree may be an independent risk factor for the development of atherosclerosis. Focusing on hypertension as a cardiovascular risk factor, our results are in agreement to studies in obese children [2]. Associations of systolic blood pressure and IMT were found for both sexes. Furthermore the results of the multiple regression analysis indicate that especially in boys systolic blood pressure should be considered as a predictor for increased IMT. Earlier reports [9] described that associations between childhood risk factors and adult carotid IMT are also strongest in young male. Our results are interesting also with regard to studies of the Cardiovascular Risk in Young Finns Study on endothelial dysfunction. Juonala et al. [10] reported that in male subjects (age 12–18 years), the level of systolic blood pressure was inversely related to adulthood endothelial-dependent flow-mediated dilatation and predicted impaired endothelial function 21 years later in adulthood.

4.1. Limitations of the study

Due to the small number of participants ($n < 16$) percentiles for age group 16/17 years in boys and girls were not calculated. The assessment of IMT values for the pediatric population has limitations in the age group 6/7 years. The theoretical axial resolution of the Loqiq Book XP with a 10 MHz transducer is approximately 0.25 mm. This implies that if the IMT is thinner the leading edges of the two echo interfaces from far wall intima and adventitia respectively cannot clearly be separated and measurements of the IMT are therefore not reliable. Since some of the measured IMT values in the youngest age group (6/7 years) were close to these technical limitations, this age group was excluded from the study sample. A transducer of higher resolution would be more appropriate in future studies.

Tanner scores were not obtained in the study participants. The pubertal stage of the children is therefore uncertain. The analysed sex differences could be explained by the effect of sex hormones. This study focused on non-invasive diagnostics in healthy children, invasive cardiovascular risk factors such as serum lipids, glucose level and markers of inflammation were not assessed.

5. Conclusions

The results of this study provided reference values of IMT for both sexes for the age groups 8/9, 10/11, 12/13 and 14/15 years. Those sex differences are remarkable especially in the pubertal phase. Since in girls a continuous IMT increase could be documented with increasing age, in boys a stagnation of IMT was assessed at the age of puberty. The non-invasive sonography of IMT was easy to perform and well tolerated. IMT is affected by sex, age, body size, weight. Cardiovascular risk factors such as BMI and body fat were associated with IMT in the female study population. Of particular importance, especially in cardiovascular health prevention is the positive correlation between IMT and systolic blood pressure for both sexes. Systolic blood pressure as the main predictor of IMT should be given careful attention in boys and should be addressed further in future studies.

The results underline that early non-invasive cardiovascular prevention is important and future research should focus on sex-specific prevention concepts, in particular, since risk factors are being tracked into adulthood [5]. IMT age- and sex-specific percentiles for a healthy pediatric population and the promotion of IMT sonography as an additional surrogate marker next to established invasive markers of cardiovascular risk factors is the main benefit of our efforts for further studies and extension to previous reports [14,15].

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.atherosclerosis.2009.03.016.

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3 Arterial structure, atherosclerotic process and exercise

Exercise is a sub-category of physical activity, which is planned, structured and repetitive with the objective of increasing one or more components of physical fitness. Physical fitness has been defined as “the ability to carry out daily tasks with vigor and alertness, without undue fatigue and with ample energy to enjoy leisure-time pursuits and to meet unforeseen emergencies”[42].

A number of measurable components do contribute to physical fitness. Those are either health-related or skill-related fitness components. The health-related fitness components are: Cardiorespiratory endurance, muscular endurance, muscular strength, body composition and flexibility. Skill-related fitness is defined with the components of agility, balance, coordination, speed, power and reaction time[42].

3.1 The antiatherosclerostic effect of exercise in adults

The effects of exercise on coronary risk factors are multifactorial. It is likely that the atherosclerotic process is affected through a positive effect of certain cardiovascular risk factors. Studies in primary prevention in adults describe the basis for the value of exercise intensity or calorie expenditure[43-49]. Further there are significant prospective studies on physical conditioning and cardiovascular mortality in adults[43,45,46,48-50]. Those studies reflect higher death rates in individuals with low conditioning level. A typical example of one of these facts is the Aerobics Center Study[45] in which there was a strong inverse relation between physical conditioning and mortality in prospective studies of men and women[44,45,50]. Conditioning was determined by maximal exercise test on a treadmill. Treadmill time distributions within age-specific and sex-specific groups were used to assign individuals to low, moderate and high physical conditionings. These early studies were done between 1970 and 1982. Follow-up for mortality was from the date of baseline examination approximately 8 years on average. The first mortality report from this study was on 10.224 men and 3120 women with no history of myocard infection, stroke, hypertension or diabetes at baseline[45]. Blair and colleagues described the cardiovascular disease mortality for low, moderate and high conditioning groups[44]. The age-adjusted relative risks for low compared with high physical conditioning are approximately nine in women and eight in men.

Other studies on the relationship between physical conditioning and cardiovascular disease show results similar to mortality studies[51,52]. The relationships between physical conditioning and cardiovascular mortality persist, even after extensive multivariate analysis for various variables.

The intensity of exercise training for cardiovascular risk modification is variable, depending on the risk factors of coronary artery disease. High-density lipoprotein levels and high blood pressure seem to be more positively affected by high intensity exercise, whereas low and moderate intensity activity levels seem to be effective for most risk factors (triglycerides, glucose intolerance, body weight)[53]. An important aspect in atherosclerosis prevention is the fact of long-term physical activity or exercise to effect the changes because the atherosclerotic process is progressive, too.

However, modification of traditional risk factors fails to fully explain the magnitude of exercise-mediated risk reduction[54] so that it is proposed by Green and colleagues[55], that there are direct effects of exercise on the vascular wall, which confer cardioprotection via a “vascular conditioning” effect. In this context it has been described in healthy adults that IMT is associated to sedentary behavior and associated to establish cardiovascular risk factors[56].

Further studies of Sandrock and colleagues[57] described that lifetime physical activity correlates with decease of proven risk factors and a reduction of atherosclerosis in the common carotid artery. Additionally, physical activity over lifetime significantly reduces the atherosclerotic wall process. Furthermore, an inverse relationship between VO^2max and the indicators of carotid atherosclerosis could be described. The authors explained their findings that physical activity slows the progression of atherosclerosis by improving cardiorespiratory fitness. Those mechanisms were also suggested in patients with coronary heart disease[58]. The study showed for the first time that the effect of physical activity could be measured with the use of ultrasound examination in adults.

3.2 Arterial structure and function in relation to physical activity and exercise in childhood and adolescents

The positive effects of cardiorespiratory fitness and physical activity in adults lead to the speculation that those mechanisms exist in children and that an early active lifestyle improves vascular health in adulthood. It has been published that intervention strategies with physical activity could improve arterial function in youth with risk factors[59,60].

Work on healthy children is still rare and has provided contradictory findings. Schack-Nielsen and co-workers[2] showed that the amount of time 10 year-old children spent to play or participated in sports is inversely related to arterial stiffness of the aorto-radial and aorto-femoral segments. In contrast, Reed and colleagues[1] found no significant relationships between to total amount of physical activity (7-day questionnaire) and arterial compliance in 9-11 year old children.

Cross sectional studies suggest that aerobic fitness may contribute to improve arterial function in healthy children. Treiber and co-workers[3] described that aerobic fitness explained 23% of the variance in femoral FMD among children aged 11-14 years.

Performance on a 20-m-shuttle run appears to contribute to large- and small- artery compliance (15% and 7% respectively), with children who show the highest performance compared to those with the lowest performance scores[1].

There are currently no studies that assessed relationships between physical fitness and vascular structure in young children. The following study was investigated at five primary schools in and around Munich and was submitted to the International Journal of Pediatrics in January 2011 and is currently in review. The main aim of the study was to assess if IMT and health-related fitness components are associated in young children.

3.3 Pediatric prevention of atherosclerotic cardiovascular disease – is health-related fitness related to carotid intima-media thickness in young school children?

3.3.1 Introduction

Children are at increased risk of atherosclerotic cardiovascular disease when overweight and physically unfit[61]. Being overweight in childhood and adolescence has been linked with increased rates of hypertension[62], type II diabetes and early atherosclerotic lesions[63]. Obesity and hypertension[59,64,65] are key issues for the development of subclinical cardiovascular disease[63], in addition a tracking of these risk factors of later cardiovascular disease into adulthood has been described[66].

Increasing the level of physical activity is an important component of childhood obesity management. Furthermore, regular physical activity may have independent effects on reducing the risk of coronary heart disease, hypertension and diabetes mellitus[67]. As such, physical activity seems to be a protective factor. However, controversy still exists in literature, whether fitness and fatness are independently related to cardiovascular risk in children[68,69]. Parizkova and colleagues[70] found that overweight children who show a good fitness level are at reduced risk for morbidity compared to their poorly fit peers. It is established knowledge that children need a multitude of physical activity to develop sport motor abilities and fitness, necessary for healthy physical development. In this context, health-related fitness, defined as cardiorespiratory endurance, body composition, muscle strength and flexibility[71] is of particular interest. Since health-related fitness is closely associated with cardiovascular disease mortality itself[72] and secondly, it seems to decline in children and adolescents of Western countries[73]. The sedentary lifestyles of German preschool children are increasing, in consequence sport motor deficits, less physical fitness, and psychological abnormalities e.g. depression have been observed[74,75].

Next to the analysis of the individual health-related fitness status it is of utmost importance to detect early signs of atherosclerotic vascular wall changes. Direct signs of early arterial structural changes can be detected by non-invasive sonographic visualization of the intima-media complex of blood vessels, especially the common carotid artery (IMT). This parameter represents a marker of subclinical atherosclerosis because it correlates with vascular risk factors[76] and further relates to coronary artery disease in adults. IMT is also used as a surrogate marker of cardiovascular health[4]. Results of the Cardiovascular Risk in Young Finns study revealed that risk factors such as body mass index (BMI), systolic and diastolic blood pressure, total cholesterol, triglycerides and LDL-C levels when determined in adults[77].

As ultrasound testing is reproducible, non-invasive and not painful, it is an ideal procedure for CVD screening for the young[38]. In a recent study, IMT reference values for a German healthy pediatric population have been published for boys and for girls[5].

According to the American Heart Association[78], the earlier cardiovascular risk factors are controlled, the greater is the potential for deferring the onset of coronary heart disease. The use of sonography could provide a valuable supplement in especially high-risk pediatric patients and may also serve as an additional parameter of cardiovascular health prevention.

It is currently not known if health-related fitness correlates with directly assessed IMT in youth. Boreham and colleagues[79] showed that there are modest but significant relationships between adolescent fitness and predictors of cardiovascular disease risk, such as skin fold thickness, serum total cholesterol and HDL cholesterol ratio, in early adulthood. Findings by Davis and co-workers[80] show an association between carotid IMT and coronary calcification in young adults who participated in the Muscatine Study and suggested that carotid ultrasound measurement could be useful in identifying young adults at risk for premature coronary atherosclerosis.

Especially when considering long-term primary prevention, the importance of health-related fitness in relation to cardiovascular health, obesity prevention and blood pressure is valuable compared to the influence of body composition on the cardiovascular system[79,81]. The early monitoring and screening of risk factors towards the detection of early vascular changes of arteries is important since primary prevention will be most effective if progress towards the control of these risk factors begins in youth[79].

Focusing on non-invasive diagnostic parameters of atherosclerotic cardiovascular disease risk and as an extension to previous studies, the sonography of IMT was integrated in this study.

The main objectives of the present study were to investigate, if health-related fitness is associated to IMT. In that context the possible relationships between body composition, blood pressure and IMT were analyzed, taking sex differences into account.

3.3.2 Methods

A total of 197 pupils from Munich primary schools (boys and girls, age 6-10 yrs) participated in the study. Sonographic data from 137 participants were included. The children were randomly selected from primary schools grade one to four and participated voluntarily after written informed consents were obtained from their legal representative. The local institutional Ethics Committee of the Technische Universität München, Faculty of Medicine, approved the study (protocol number 1162/04). The study was carried out on two weekends in the same Munich primary school. The children were scheduled in groups of 25 children, starting off with the anthropometric data collection and sonography in the morning, followed by the physical fitness tests on the same day in the afternoon. On both weekends the staff members were the same, whereas trained medical doctors were responsible for the anthropometric data collection and sonography and trained sport scientists carried out the health-related fitness test battery.

Anthropometric data collection

Body weight was measured to the nearest 0.10 kg using an electronic body weight scale (SECA 702), light dressed in T-shirts and shorts. Height was measured to the nearest mm in bare using SECA 702. Body mass index (BMI) (kg/m^2) was calculated from the ratio of $weight/height^2$. The percentage of body fat was examined using FUTREX 6100/XL. Near-infrared measurement was performed by placing the Futrex sensor on the non-access upper arm for several seconds, after login of the required individual data (sex, age, weight, height) as described and validated for children by Cassady and colleagues[82]. Each subject was measured three times. The mean value was used for further statistical analysis. After 15 min rest systolic and diastolic blood pressure were measured (Riva Rocci) twice at the right arm in a supine position (legs not crossed) using a calibrated, age-specific sphygmomanometer.

Ultrasound measurement of the IMT of the A. carotis communis

In a recumbent position with slightly reclined neck, the two-dimensional ultrasound examination of the right common carotid artery was performed with a 10 MHz linear transducer (Logiq Book XP, GE Germany) following a standardized protocol. The carotid tree was first scanned with the transducer positioned at the lateral side of the neck and then rotated by 90° to achieve a longitudinal image of the carotid artery. The lumen of the common carotid artery and the carotid bulb were maximized with gain settings to optimize image quality. The image included the beginning of carotid bifurcation, the common carotid artery, and was focused on the posterior (far) wall. The distance between the lumen-intima interface and the media-adventitia interface reflects the intima-media complex, which was displayed horizontally over the maximal possible distance. A moving scan with of 5 seconds was recorded and stored in digital format for offline analysis. From the 5-seconds clip image, three best quality end systolic-frames of each subject were selected and used for offline analysis[5].

IMT was measured offline according to the standardized protocol by semi-automated edge detection using a measurement computer software package (Sigma Scan Pro 5.0) previously described by Sander and co-workers[83]. In brief, IMT measurements were performed 8-18 mm proximal to the carotid artery bifurcation on a strictly horizontal segment. On the 1-cm segment, 11 measurements of the IMT of the far wall were automatically attempted at 1-mm increments, with the image analysis system and the IMT of the segment was estimated as the mean of these 11 measurements. This approach has been sufficiently evaluated for superficial arteries in adults[84].

<u>Health-related physical fitness diagnostic</u>

To assess health-related physical fitness all subjects performed valid and reliable tests from standardized sport motor fitness test batteries: “sit-ups” to assess abdominal and endurance strength[85], “bent-arm hang” to assess upper trunk and endurance strength[86], “sit-and-reach” to assess harmstring, gluteal and lower back musculature flexibility[86,87] and a “6-minute run” to assess cardiorespiratory endurance[88,89].

All subjects performed the fitness tests, adjusted to subject’s age. All measures were conducted in a school gymnasium, provided with standardized gymnastic facilities. After a standardized 10 min warm-up program the tests were performed in a defined order, starting off with “sit-ups”, followed by “sit-and-reach test” and “bent-arm hang”. Finally, the “6-minute run” was performed last in groups of 10 children. There was adequate time for each child to fully relax between the tests. The objective for the composition of the used sport motor test battery was to analyze the different components of health-related fitness. The tests were chosen because of the ease of their administration to large numbers of subjects and its choice of reliable and valid measures for a general healthy pediatric population. The participants received verbal encouragement from the investigators to achieve maximum performance. Brief descriptions of the tests follow below:

Sit-ups – assessment of abdominal and endurance strength

The children were instructed to keep arms folded across the chest, place feet about 38 cm from the buttocks, touch the elbows to thighs on the upward position, and touch midback to mat on the downward position. For testing purposes the participants' feet were held down by another participant and floor mats were provided for comfort. The test measures abdominal strength and endurance. Children age 6-10 years performed a maximum number of achievable sit-ups in 40 sec[85].

Bent-arm hang – assessment of upper trunk muscular endurance strength

The bent-arm hang was tested and instructed as previously described in the Handbook for Eurofit Tests of Physical Fitness[86]. The child maintained a bent-arm position while hanging on a bar with a forward grip at shoulder width. The time in tenth of a second was the score.

Sit-and-reach – assessment of harmstring, gluteal and lower back musculature flexibility

One of the most commonly used field tests for hamstring, gluteal and lower back musculature flexibility in children is the sit-and-reach test. It has one of the highest test-retest reliabilities (r=0.89 to 0.97) for measures of flexibility[87]. With legs fully extended, children were asked to reach forward three times and hold position on maximal reach. Research assistants recorded farthest reach to the nearest cm.

6-minute run – assessment of cardiorespiratory endurance

Endurance performance was tested using the 6-minute run field test. The test is valid, objective and reliable for school children and correlated with results of treadmill testing (r=0.39); the shuttle run (r=0.88) and metabolic parameters such as lactate (r=0.92)[89,90]. For this study participants were instructed to run for 6 minutes completing the longest distance possible on a 250 meters course by either running or occasionally walking. Research assistance counted the laps, motivated the children during the test, and recorded the distance in meters.

Questionnaire:

The children filled out a validated questionnaire form the German Health Interview and Examination Survey for Children and Adolescents[90]; the youngest children were assisted by their parents. Questions included information about sports club participation and general physical activity during leisure time as well as hours of school physical education per week. Information about the sports club participation in hours per week was included in the study.

Statistical analysis

Data were encoded, checked and subsequently analyzed using SPSS 17.0. To adjust children's BMI for sex and age, the observed BMI values were transformed to sex- and age-specific z-scores established by the World Health Organization (WHO) (http://www.who.int/growthref/en)[91]. Hypertension was defined with regard to sex and age by values above the 95th percentile of the International Task Force[92]. IMT values were classified into three groups following German age- and gender-specific reference values[5]: < 25th percentile, ≥ 25th to <75th percentile and values > 75th percentile. Results of the health-related fitness tests were classified due to German references values, which were assessed in the German Health Interview and Examination Survey for Children and Adolescents, offering nationwide representative data of 4.529 children on motor fitness. The results are divided into severely disturbed, moderately disturbed, normal, good and very good performance[90,93].

Normal distribution was tested using Kolmogorov-Smirnov Test. Since data show a normal distribution, results are presented as means +/- standard deviation (SD). To identify differences in gender Students t-test for two independent sample groups were calculated. Relationships between atherosclerotic cardiovascular risk factors and health-related physical fitness were analyzed with Pearson correlation analysis with the relationship illustrated using Pearson's correlation coefficient (r).

Multiple linear regression analysis was performed with age-adjusted IMT as dependent variable and BMI, total percentage of body fat, systolic and diastolic blood pressure, each health-related fitness component adjusted for age and body fat for both sexes. All covariates included in the model were tested for interaction with each other. Because the variance inflation factor (VIF) was <5 and condition indices were <15 no correction for colliniarity of the data was necessary[94]. Values of p<0.05 were considered statistically significant.

Means and standard deviations (SDs) for differences between observers were calculated. The inter- and intra-observer error (s) was calculated according to the formula $s = SD/\sqrt{2}$. The coeffcient of variation (CV) describes the difference as a percentage of the pooled mean value $\bar{x}$ and was calculated according to the formula:

$$CV = \frac{s \cdot 100\,\%}{\bar{x}} \quad .$$

3.3.3 Results

The characteristics of all participants (n=197; 84 boys, mean age 8.68 ± 0.93 years and 111 girls, mean age 8.57 ± 0.95 years) are shown in Table 1. None of the children showed a pathologically increased IMT and no plaques were detected. The IMT ultrasound examination time was approximately 5 min/patient; the offline analysis 8 min/picture. The intra-observer variability presented as the coefficient of variation (CV) was 2.42% (n=132, deviation mean 0.012mm; r=0.849). The inter-observer variability described as CV was 1.71%, (n=75, deviation mean 0.013mm; r=0.780).

There were no significant (p=0.109) differences of IMT between boys and girls. In detail, 8.3% (n=8) of the boys and 7.2% (n=8) of the girls had an age-specific IMT <25th percentile; 47.6% (n=40) boys and 66.7% (n=74) girls showed IMT values ranging from ≥25th to <75th percentile and 6% (n=5) of the boys versus 2.7% (n=3) of the girls showed IMT values >75th age percentile.

Boys were significantly taller and showed significantly higher percentage of body fat. With regard to age and gender 8.3% (n=7) of the boys and 10.8% (n=12) girls were overweight (p=0.564). 2.4% (n=2) of the boys were hypertensive (systolic) and all girls had a normal blood pressure (p=0.103). Boys and girls stated 1.5 hours/week of physical education in school. Boys additionally reported 2.57 ± 1.46 hours of exercise in a sport club, whereas girls reported a participation time of 2.50 ± 1.47 hours of sport activities in sports clubs (Table 1).

Table 1 Subject characteristics; number of subjects, means, standard deviations and the representation of results between boys and girls.

Values of $P < 0.05$ were considered statistically significant.

Abbreviations: BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; IMT: Intima-media thickness of the A. carotis communis.

Subject Characteristics	**Boys**			**Girls**			***P* value**
	N	Mean	SD	N	Mean	SD	
Age [years]	84	8.68	0.93	111	8.57	0.95	0.417
Height [cm]	84	137.17	7.11	111	135.0	7.58	0.045*
Weight [kg]	84	31.79	6.56	111	30.78	5.75	0.255
BMI [kg/m²]	84	16.75	2.19	111	16.79	2.21	0.915
BMI z-scores	84	0.28	1.15	111	0.29	0.98	0.950
Body fat [%]	84	22.96	2.90	111	18.40	2.69	<0.001**
SBP [mmHg]	84	103.92	8.84	111	103.24	9.60	0.406b
DBP [mmHg]	84	71.27	9.07	111	69.20	8.52	0.113
IMT [mm]	52	0.507	0.046	85	0.494	0.042	0.109
Reported sport club participation [hours/week]	82	2.57	1.46	105	2.50	1.47	0.632

Results of the health-related fitness test performances in boys and girls are presented in Table 2 and Figures 1-4. Boys performed significantly better in the upper trunk muscular endurance strength test assessed by bent-arm hang. Girls test performance was significantly better in harmstring, gluteal and lower back musculature flexibility, assessed by the sit-and-reach test. No significant differences in performance revealed between boys and girls in abdominal muscular endurance, examined by sit-ups and cardiorespiratory endurance, examined by the 6-minute run.

Table 2 Health-related fitness performances in boys and girls.

Data presented as mean and standard deviation (SD), minimum and maximum of performances as well as the performances in percentiles. Significant differences between boys and girls are calculated and presented. The level of significance was defined as $P < 0.05$.

								Percentiles				
			Mean	SD	Minimum	Maximum	*P* Value	10th	25th	50th	75th	90th
Sit and reach [cm]	Boys	84	-1.32	6.45	-23.0	13.0	<0.001	-9.00	-5.00	.00	3.00	5.60
	Girls	111	2.91	5.78	-11.0	15.0		-5.00	-.75	3.00	6.80	12.00
Bent-arm hang [sec]	Boys	84	13.08	8.84	1.6	45.0	0.049*	3.99	6.02	10.00	18.00	25.47
	Girls	111	10.94	6.21	1.4	27.6		3.48	6.48	10.00	14.50	21.52
Sit-ups [n]	Boys	84	21.24	6.22	2.0	40.0	0.086	14.00	16.25	21.00	25.00	28.50
	Girls	111	19.57	6.35	5.0	40.0		11.10	16.00	19.00	23.00	26.90
6-minute run [m]	Boys	84	943.9	111.1	675.0	1175.0	0.166	800.0	846.2	950.0	1010.0	1100.0
	Girls	111	923.0	98.5	675.0	1130.0		788.0	850.0	900.0	1000.0	1050.0

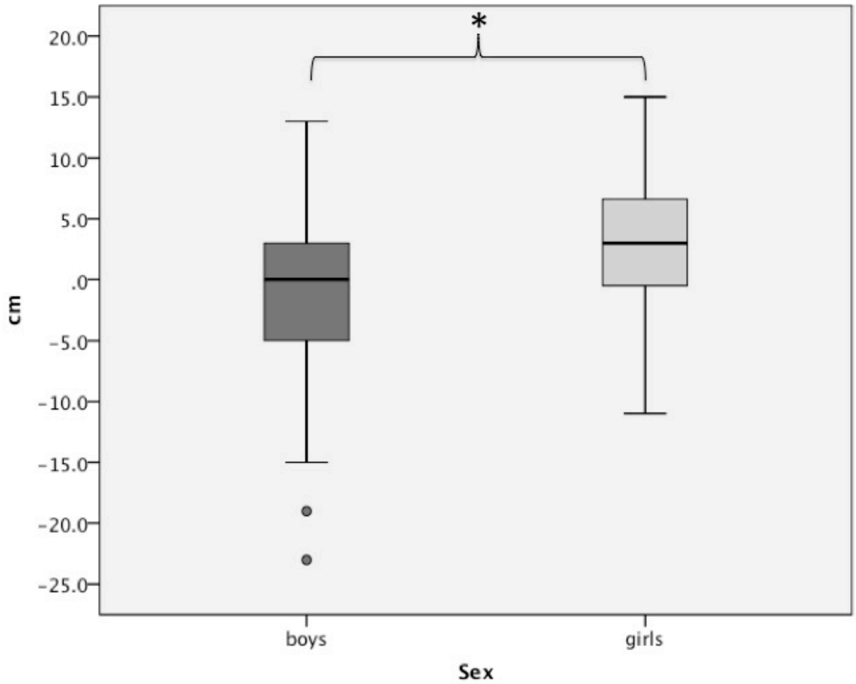

Figure 1 Results of the sit-and-reach test (in centimeters) for boys and girls.
Values of $P < 0.05$ were considered statistically significant.

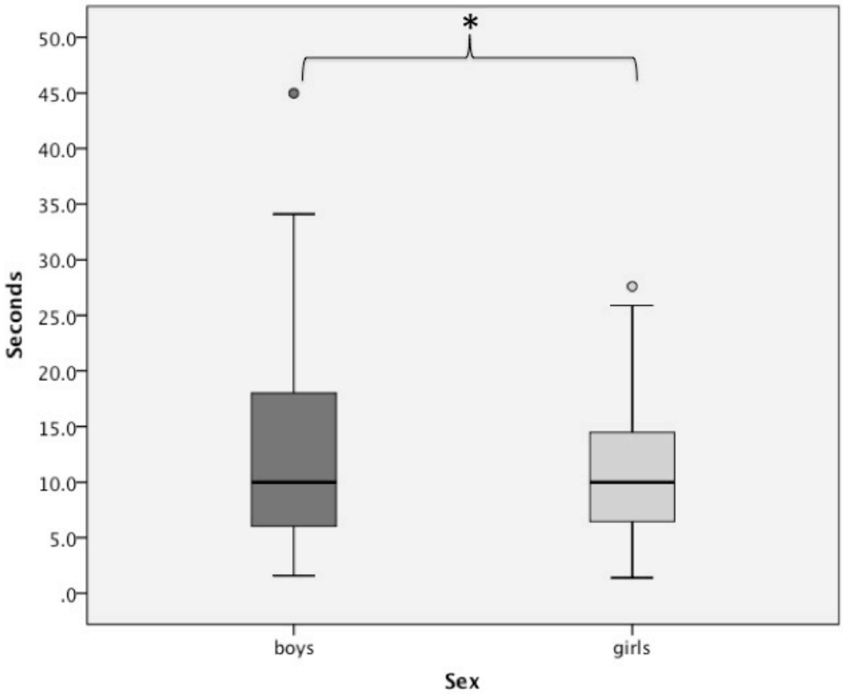

Figure 2 Results of the bent-arm hang (in seconds) for boys and girls.
Values of *P* < 0.05 were considered statistically significant.

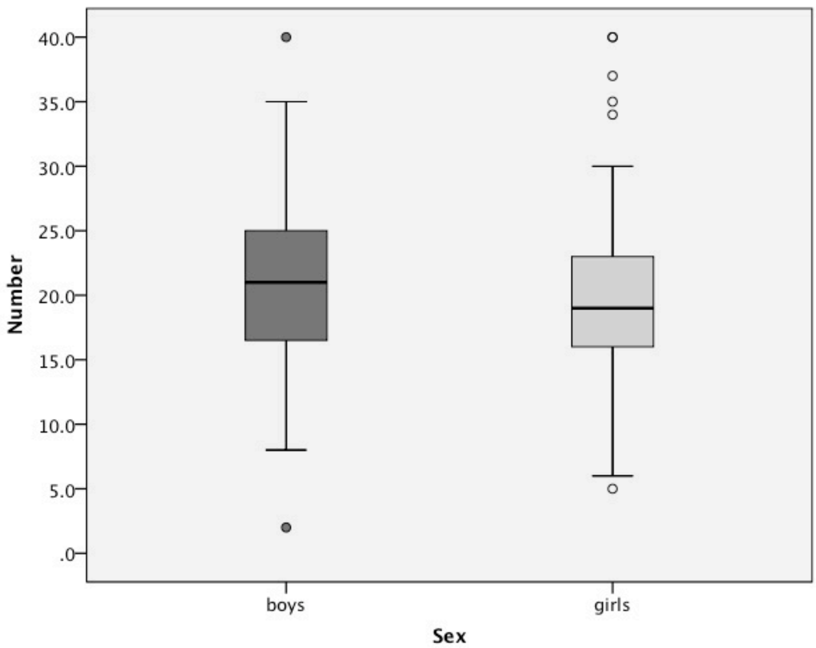

Figure 3 Results of the performed number of sit-ups presented for boys and girls.

Values of *P* < 0.05 were considered statistically significant.

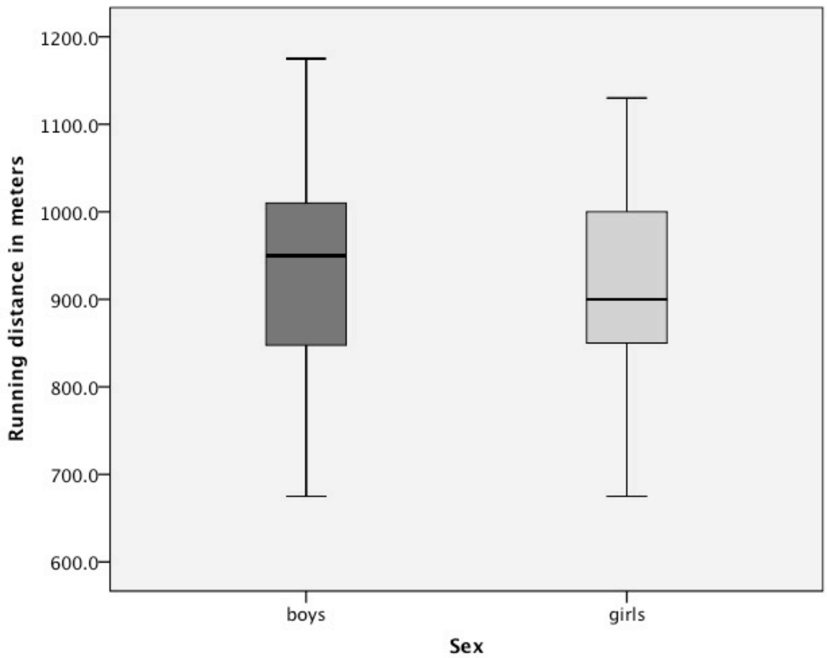

Figure 4 Results of the 6-minute run (in meters) for boys and girls.

Values of $P < 0.05$ were considered statistically significant.

Table 3 displays health-related fitness components of the study group in comparison to national German reference values[89,93]. In all fitness tests, more than 50% of the children performed very good, good and normal results. An exception was the endurance capacity in boys, where only 48.8% of the boys performed very good, good and normal results.

Table 3 Results of the studied children, evaluated according to German national reference values, depending on the test performance, age and sex.

Abbreviations: BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; IMT: Intima-media thickness of the A. carotis communis

		Boys		Girls	
		N	%	N	%
Sit-and-reach [cm]	very good	3	3.8%	11	10.2%
	good	15	18.8%	24	22.2%
	normal	31	38.8%	48	44.4%
	moderately disturbed	25	31.3%	23	21.3%
	severely disturbed	6	7.5%	2	1.9%
Sit-ups [n]	very good	9	10.7%	18	16.4%
	good	17	20.2%	22	20.0%
	normal	22	26.2%	35	31.8%
	moderately disturbed	15	17.9%	19	17.3%
	severely disturbed	21	25.0%	16	14.5%
Bent-arm hang [sec]	very good	1	1.2%	0	.0%
	good	22	26.2%	31	27.9%
	normal	34	40.5%	58	52.3%
	moderately disturbed	22	26.2%	15	13.5%
	severely disturbed	5	6.0%	7	6.3%
6-minute run [meters]	very good	11	13.1%	26	23.4%
	good	14	16.7%	17	15.3%
	normal	16	19.0%	23	20.7%
	moderately disturbed	18	21.4%	36	32.4%
	severely disturbed	25	29.8%	9	8.1%

The main emphasis of the study was to assess relations between health-related fitness and IMT taking sex into account. The results of these correlations and further the relationships between traditional cardiovascular disease risk factors are shown in Table 4.

The Pearson's correlation analysis revealed that there was a lack of significant relationships between health-related fitness and IMT in either boys or girls.

The most significant association between health-related fitness and body composition could be demonstrated for body fat. The results showed an inverse relationship between the total percentage of body fat and abdominal muscular endurance strength (sit-ups) for boys and girls, additionally to upper trunk muscular endurance strength (bent-arm hang) and cardiorespiratory endurance capacity in boys only. For girls, there was a negative relationship between the total percentage of body fat and harmstring, gluteal and lower back muscular flexibility (sit-and-reach test).

BMI was inversely related to upper trunk muscular endurance strength and cardiorespiratory endurance capacity in boys. In girls, a negative correlation between BMI and harmstring, gluteal and lower back muscular flexibility could be described.

No relationships between health-related fitness and blood pressure could be verified for boys and girls. Diastolic blood pressure was inversely related to abdominal and upper trunk muscular endurance strength.

Table 4 Relationships between non-invasive cardiovascular risk factors and health-related fitness in boys and girls.

Pearson correlation coefficients and *P* values are describing the relationship. The level of significance was defined as $P < 0.05$.
Abbreviations: BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; IMT: Intima-media thickness of the A. carotis communis.

			Sit-ups [n]	Bent-arm hang [sec]	Sit-and-reach [cm]	6-minute run [m]
IMT [mm]	Boys	r	-0.007	-0.154	0.031	-0.055
		P value	0.960	0.274	0.828	0.697
	Girls	r	0.011	-0.017	-0.043	-0.030
		P value	0.924	0.874	0.696	0.789

Continuation of Table 4			Sit-ups [n]	Bent-arm hang [sec]	Sit-and-reach [cm]	6-minute run [m]
BMI [kg/m²]	Boys	r	0.092	-0.292**	-0.018	-0.313**
		P value	0.404	0.007	0.873	0.004
	Girls	r	0.014	-0.269**	-0.223*	-0.251**
		P value	0.883	0.004	0.021	0.008
Body fat [%]	Boys	r	-0.237*	-0.214	-0.119	-0.325**
		P value	0.031	0.052	0.287	0.003
	Girls	r	-0.195*	-0.208*	-0.246*	-0.053
		P value	0.042	0.028	0.010	0.579
SBP [mmHg]	Boys	r	-0.197	-0.035	0.173	-0.006
		P value	0.072	0.755	0.119	.0954
	Girls	r	-0.161	-0.016	-0.063	-0.051
		P value	0.094	0.871	0.516	0.599
DBP [mmHg]	Boys	r	-0.260*	-0.220*	0.084	-0.128
		P value	0.017	0.044	0.452	0.246
	Girls	r	-0.130	-0.127	-0.045	-0.158
		P value	0.177	0.185	0.644	0,099

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Table 5 summarizes the relationships between IMT and traditional CV risk factors in healthy children. In girls only, the analysis of IMT and anthropometric data resulted in significant relationships between IMT and body composition, namely weight, BMI and body fat. Additionally in girls, the total percentage of body fat was shown to be the only significant predictor variable (ß=0.364, p=0.003) for IMT (F [2.82] =5.415, p=0.006) adjusted R square = 12%). No relationships were evident in boys.

Furthermore weight was significantly related with age, height, body fat and systolic blood pressure for both genders. Additionally in boys a positive correlation between, weight and diastolic blood pressure could be found.

A significant relationship also existed between BMI and the total percentage of body fat, BMI and systolic as well as BMI and diastolic blood pressure.

Analysis of total percentage of body fat resulted in significant correlations between weight; BMI; and systolic blood pressure for boys and girls. Additionally in boys, the Pearson's correlation analysis revealed significant relationships between the total percentage of body fat and diastolic blood pressure.

Table 5 Pearson correlation coefficients (r) and *P* values assessing the relationship between non-invasive CVD risk factors in boys and girls.

Pearson correlation coefficients and *P* values are describing the relationship. The level of significance was defined as *P* < 0.05.
Abbreviations: BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; IMT: Intima-media thickness of the A. carotis communis.

			Age [years]	Height [cm]	Weight [kg]	BMI [kg/m²]	Body fat [%]	SBP [mmHg]	DBP [mmHg]
IMT [mm]	Boys								
		r	0.119	0.081	0.030	0.027	0.012	0.129	0.111
		P value	0.401	0.566	0.835	0.852	0.933	0.363	0.433
	Girls								
		r	0.120	0.153	0.275*	0.249*	0.338**	0.135	0.159
		P value	0.275	0.162	0.011	0.022	0.002	0.221	0.149

	Continuation of Table 5		Age [years]	Height [cm]	Weight [kg]	BMI [kg/m²]	Body fat [%]	SBP [mmHg]	DBP [mmHg]
Weight [kg]	Boys	r	0.412**	0.784**	1	0.882**	0.901**	0.355**	0.353**
		P value	0.000	0.000		0.000	0.000	0.001	0.001
	Girls	r	0.386**	0.702**	1	0.811**	0.925**	0.393**	0.150
		P value	0.000	0.000		0.000	0.000	0.000	0.117
BMI [kg/m²]	Boys	r	0.217*	0.413**	0.882**	1	0.784**	0.302**	0.356**
		P value	0.047	0.000	0.000		0.000	0.005	0.001
	Girls	r	0.017	0.160	0.811**	1	0.733**	0.361**	0.244*
		P value	0.862	0.093	0.000		0.000	0.000	0.010
Body fat [%]	Boys	*r*	0.399**	0.703**	0.901**	0.784**	1	0.304**	0.362**
		P value	0.000	0.000	0.000	0.000		0.005	0.001
	Girls	r	0.415**	0.660**	0.925**	0.733**	1	0.395**	0.121
		P value	0.000	0.000	0.000	0.000		0.000	0.209

3.3.4 Discussion

To our best knowledge this was the first pediatric study that combined the sonography of IMT and objectively measured health-related fitness components next to traditional non-invasive atherosclerotic cardiovascular risk parameters such as body composition and blood pressure to assess relationships in young children. Moreover, the study investigated if health-related fitness could predict early vascular wall changes. An early approach was chosen since cardiovascular prevention will be most effective if control of these risk factors begins in youth[22].

The principle findings of this cross-sectional examination of the relationships between risk factors, particularly health-related fitness and carotid IMT in healthy, generally non-obese, young children was first, physical fitness was not related to IMT and second the total percentage of body fat revealed as a predictor for IMT in girls only. Further IMT was not associated to any other cardiovascular risk factors in boys and girls.

In this investigation the IMT analysis were based on the far (posterior) wall of the intima-media complex as established[95], using a linear transducer of 10 MHz[60] . The IMT values of boys, lower than the age-specific 25th percentile, corresponded to previous reports[60,96]. 66.7% of the girls and 47.6% of the boys showed IMT values between the 25th and 75th percentile. Three girls (2.7%) and five boys (6%) showed values higher than their age-specific 75th percentile. The values above the 75th percentile corresponded to measurements of De Groot and co-workers[97] for healthy controls of greater age (n=44, mean age 14.9 ± 2.8 years of 0.53 ± 0.03 mm) and therefore are slightly increased for the age of 8/9 years. However, plaques were not detected in any of the children[98]. The comparison of IMT values is complex since diverse ultrasound frequencies were utilized in previous studies[96,99].

In the context of early atherosclerotic risk screening we addressed overweight and hypertension as well as low health-related fitness as risk factors[64,65]. The results in the present study reveal sex differences, in which 10.8% of the girls and 8.3% of the boys were overweight. Those figures are somewhat lower than the national average of 15% in 7-11 year old boys and girls[100]. Two overweight boys were hypertensive and all other children were normotensive.

The results on traditional cardiovascular risk factors demonstrated that BMI and body fat were related to cardiovascular risk factors such as systolic and diastolic blood pressure in both genders. These findings highlight the importance of early prevention of overweight and hypertension even in healthy children and especially relevant when childhood obesity is increasing[101] and physical fitness is decreasing[73].

The sports club participation of the studied children was generally high, whereas boys showed slightly higher but not significantly higher participation than girls[69,88]. Those sex differences also revealed differences in health-related fitness. Boys performed better in abdominal strength, upper trunk strength and endurance capacity than girls. Therefore, girls demonstrated 23% better hamstring, gluteal and lower back musculature flexibility than boys. These outcomes with regard to sex differences and performance are consistent with previous reports[69,74,102,103].

However, we could not assess significant relationships between IMT and health-related fitness parameters such as abdominal and upper strength muscular endurance, flexibility and cardiorespiratory endurance in primary school children. Currently little is known regarding a possible relationship of IMT and health-related physical fitness in childhood. An initial intervention study indicated a salutary effect of exercise on arterial structure and function in obese youth. After supervised exercise training the cardiovascular risk profile ameliorated, carotid IMT and endothelial function improved[59]. However, the specific role of exercise was not exactly clear, since changes in body weight, body fat and lipid profiles were concomitant.

In an analysis of 47 healthy children, ages 5-10 years, Abbott and colleagues[104] found that the level of physical activity was significantly related to brachial artery flow-mediated dilatation.

The pediatric population in our study was healthy, physically active and IMT was not increased. With regard to German national reference values it can further be stated that the fitness level of the present study population was not impaired. Furthermore the activity level was generally high[69,88]. Due to this fact it is may be not surprising that there were no relationships between health-related fitness and IMT. Since it has been previously described that a healthy endothelium protects vessel walls from inflammation and prevents adhesion of platelets[14].

To further understand the role of health-related fitness in relation to vascular endothelial health, it could be suggested to analyze biomarkers of endothelial dysfunction and arterial compliance as possible more sensitive functional parameters in contrast to IMT, in relation to fitness and physical activity in future pediatric investigations.

Limitations of the study

Our study has some limitations. We only examined children of primary schools from Munich schools. Therefore the group was homogeneous and the results cannot be extrapolated into other age groups or populations. This study focused on non-invasive diagnostics in healthy children, invasive cardiovascular risk factors such as serum lipids, glucose level and markers of inflammation were not assessed. Furthermore Tanner scores were not obtained in these young children.

3.3.5 Conclusions

A new aspect in this cross-sectional examination in healthy, generally non-obese, young children was the combination of carotid IMT sonography in relation to objectively measured health-related fitness parameters next to traditional non-invasive atherosclerotic cardiovascular risk parameters such as body composition and blood pressure. The new findings revealed no relationships between IMT and health-related fitness. In girls only, the analysis of IMT and anthropometric data resulted in significant relationships between IMT and body composition, namely weight, BMI and the total percentage of body fat was shown to be the only significant predictor variable for IMT.

4 Early atherosclerotic wall changes in overweight and obese children and adolescents and the role of physical fitness.

4.1 Introduction

Overweight and obesity prevalence are increasing in children worldwide[105-108]. Since the early 1990s in some countries it has doubled, in other countries it has tripled[109]. The World Health Organization has declared obesity as a global epidemic. Using international definitions, at least 10% of the school children worldwide are overweight or obese, whereas the Americans are leading (32%), followed by Europe (20%) and after that the Middle East (16%)[107]. In Germany 8.7% of the children and adolescents between 3 and 17 years of age are overweight, 6.3% are obese. Differences in overweight and overweight trends also occur by social class and ethical groups, emphasizing the importance of non-genetic variables[110-112].

One of the main concerns of the rise in pediatric obesity is the possible impact that this will have on adult atherosclerotic disease rates in the future. The association between child and adult obesity is complex. A review of 15 study populations described positive correlations between obesity related cardiovascular risk in childhood and adulthood[113]. Further, there is evidence, from the Bogalusa Heart Study, that children who have overweight onset before the age of eight are at significantly increased risk of obesity in adulthood[114]. Understanding the implications of such risk factors is of considerable interest for the prevention of atherosclerotic cardiovascular disease in adulthood[29].

Besides the clinical evidence, overweight and obesity cause a great financial burden for the health care systems in Europe. For the year 2003, Knoll and Hauner[115] stated direct health cost of 85.71 Million Euros and in addition 13.3 milliard Euros for obesity associated comorbidities.

Emphasizing the clinical evidence, cardiovascular disease has been described as the major complication of overweight and obesity[116]. Next to cardiovascular comorbidities (hypertension, left ventricular hypertrophy, atherosclerosis); also metabolic (Type 2 diabetes mellitus, the metabolic syndrome); Orthopedic (Slipped capital femoral epiphysis); Psychological (depression, quality of life); Neurological; Hepatic; Pulmonary (obstructive sleep apnea. asthma); and Renal comorbidities have been described[117].

The mechanism behind is multifaceted and mainly explained by the adipose tissue. Adipose tissue is an active endocrine and paracrine tissue that releases mediators such as leptin, adiponectin, interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), which influence next to body weight, homeostasis, insulin resistance, diabetes, inflammation and atherosclerosis[118,119].

Obesity is also inducing endothelial dysfunction, a surrogate marker of an early accelerated atherogenetic process[120,121]. Studies with cardiovascular disease risk factors have described impaired flow-mediated dilatation[122], greater stiffness[123,124,125,126] and increased IMT[60,65,127,128,129,130,131].

Even during childhood obesity increases medical problems such as cardiovascular diseases[132-134] and pre - diabetes[128]. In that context several studies in children and adolescents have detected endothelial dysfunction with risk factors for cardiovascular disease[135,136]. Further children with familial hyperlipidemia and family history of type 2 diabetes are known about increased risk for early development of vascular structural and functional pathology[137,138].

4.2 The role of health- and skill-related physical fitness in cardiovascular prevention of overweight and obese children

It is now widely accepted that atherosclerosis is a chronic disease, having its origin in childhood. Since the atherosclerotic progression covers a long phase before the development of measurable plaques are manifested[16]. Therefore, it is important to evaluate the arterial health status, by the sonography of the IMT and to further analyze the role of physical exercise and over all physical fitness in this process. Studies in adults revealed controversial results. Moreau and co-workers[139] as well as Tanaka and co-workers[140] suggested that training does not typically have an impact on IMT. Contradictory a recent study in elite athletes found consistently lower carotid wall thickness in athletes versus control subjects[141]. Findings of the Amsterdam Growth and Health Longitudinal Study described that cardiovascular fitness was an independent determinant of arterial stiffness, independently from obesity and the metabolic syndrome[142].

In obese children it has generally been stated that exercise levels of physical activity in childhood has protective effects with regard to body composition and cardiovascular disease[143]. However, overweight and obese children prefer a sedentary lifestyle, which leads to less sport motor ability and physical fitness[144].

Currently it is still unclear, if health-related and skill-related physical fitness components such as cardiorespiratory endurance, muscular strength and muscular endurance, speed, coordination and reaction time have a positive effect on the intima-media thickness in overweight and obese adolescents.

4.2.1 Objectives

The present study aimed to assess the vascular status (IMT) and health-related as well as skill-related physical fitness in overweight and obese children and adolescents compared to normal weight peers. Secondly, correlations between traditional cardiovascular risk factors, surrogate markers and physical fitness components in overweight and obese children and adolescents are calculated.

Study hypotheses

1. IMT is significantly enlarged in overweight and obese children and adolescents in comparison to normal weight peers.
2. IMT is associated to non-invasively measured traditional cardiovascular risk factors (BMI, the total percentage of body fat, systolic and diastolic blood pressure) in overweight and obese children and adolescents.
3. Obese and overweight children and adolescents have significantly impaired physical fitness compared in comparison to non-obese peers.
4. IMT and traditional non-invasive cardiovascular risk factors (BMI, total percentage of body fat, systolic and diastolic blood pressure) are significantly associated to components of health-related and skill-related physical fitness (speed of limb movements, reactive strengths, coordination and speed, coordination and reaction time, cardiorespiratory fitness, upper trunk muscular endurance strength, abdominal muscular endurance strength).

4.2.2 *Methods:*

A total of 212 children and adolescents were examined. Thereof 89 study participants attended a hospitalized intervention at the Rehabilitation Center/Clinic Gaissach, Bad Tölz/Germany and were consecutively examined in the first week after admission. Further children and adolescents from Munich secondary schools were examined. The same medical doctors and sport scientists performed the investigation.

The assessment included sonography of the A. carotis communis, distal of the carotid artery bifurcation on a segment ≥ 1 cm length (GE Loqiq Book XP. 10 Mhz linear probe). Further anthropometric data height, weight, BMI, body composition (FUTREX 6100 AL) and resting (15 min.) blood pressure were taken. Both sonography and anthropometric data collection were performed in the mornings before the sport motor fitness tests following a standardized protocol as previously described[5].

Further a self-assessed health- and skill-related physical fitness test was conducted by sport scientists and qualified staff. The tests were performed in the sport gymnasium of the Clinic in Gaissach for all hospitalized patients. For the control group the tests were performed on two afternoons in the sports gymnasium of the Faculty of Sport and Health Sciences, Technische Universität München and on short-notice had to be re-arranged to the laboratory of the Faculty of Sport and Health Sciences due to security reasons (heavy snow load on the roof of the sports gymnasium, resulted in an entrance prohibition).

Both the laboratory and sports gymnasium of the clinic were provided with standardized gymnastic facilities and were complementally equipped with the computer-based test system[145]. Due to a lack of a wall bar in the laboratory of the Faculty of Sport and Health Sciences the bent-arm hang could not be tested.

The physical fitness tests were performed in the afternoons starting off with a 10-minute warm-up program, followed by the 9-minute run on the first afternoon. On the next day, the same warm-up program was performed, followed by a pre-set test order (tapping, drop jump, complex coordination and reaction time test, a 10 m coordination run, sit-ups and bent-arm hang).

Description of the physical fitness assessment

Tapping – assessment of speed of limb movement

The aim of the test is to perform as many contacts of the force plate as possible with the right and left foot. This tapping frequency is measured 4 times during a time of 3 seconds. The tapping frequency is measured in Hertz [contacts per minute]. From the four test trails a mean value of the two best trails is calculated and used for further analysis[146,147].

Drop jump – assessment of reactive strength

The aim of the study is to jump down from a platform onto a force plate and immediately up on a second landing platform. The contact time on the force platform is measured in milliseconds [msec]. Each subject has five jumps. In between the 5 jumps a recovery time of at least 10 seconds is integrated in the test. The best jump with the shortest contact time is taken for further analysis[148].

Coordination run – assessment of coordination and speed

Light barriers are set up at the start line and finishing line within a distance of 10 meters. 5 meters in front of the start line is the preparation point for the test person. The coordination run exists of 6 squares (total lengths 3.30 meters), which are set up in a row, pairwise (one for the left foot and one for the right foot). With an interspace of 2 meters a second set up of 6 squares is set up.

The objective of the coordination run is to run through squares as fast as possible without making a step mistake, e. g right foot steps in right square, left foot steps in left square. The subject has three trails; the best trail (run time in seconds) is counted for statistical analysis[145,149].

Complex reaction test – assessment of coordination and reaction time

The computer screen is divided into 4 sections. Two sections for the hands (left and right side) and two sections for the feet (left and right side). The hardware consists of two hand plates and a force plate with two sections for the right and left foot. The hand sensor plates are set up on the table in front of the test person, the force plate is under the table. Similar to the hardware the computer screen is divided. Two white fields on the screen are standing for the hand plates and two blue fields are standing for the contact area´s for the feet. After the test start, different black signals appear on the screen in random order. The aim is to touch the hand and feet plates exactly as their combinations appear on the screen. A following image only appears after the correct repetition of the showed combination. 30 different combinations are shown. The time is counted in seconds. Each test person has three trails. The best trail is counted for further analysis[145,150].

Sit-and-reach test – assessment of harmstring, gluteal and lower back muscle flexibility

One of the most commonly used field tests for hamstring, gluteal and lower back musculature flexibility in children is the sit-and-reach test. It has one of the highest test-retest reliabilities (r=0.89 to 0.97) for measures of flexibility[87]. With legs fully extended and no shoes, the children were asked to reach forward three times and hold position on maximal reach along a ruler which was placed on the top of the box. Research assistance recorded farthest reach to the nearest cm. The differences between the feet and the tip of the longest finger was measured in cm[86,151].

9-minute run – assessment of cardiorespiratory endurance capacity

Cardiorespiratory endurance capacity was assessed in all students using a group administered timed 9-minute run. Standards of performance for youth are well established, and test re-test reliability in third grad students was 0.90. Correlations with more complex measures of fitness were estimated in the pilot phase of the CATCH study[152,153].

Bent-arm hang – assessment of upper trunk muscular endurance strength

The bent-arm hang was tested and instructed as previously described in the Handbook for Eurofit Tests of Physical Fitness[86,151]. The child maintained a bent-arm position while hanging on a bar with a forward grip at shoulder width. The time in tenth of a second was the score.

Sit-ups – assessment of abdominal and endurance strength

The children were instructed to keep arms folded across the chest, place feet about 38 cm from the buttocks, touch the elbows to thighs on the upward position, and touch midback to mat on the downward position. For testing purposes the participants' feet were held down by another participant and floor mats were provided for comfort. The test measures abdominal muscular endurance. The maximum number of achieved sit-ups in 30 seconds was counted[86,151,154].

Statistical analysis

All data were analysed in SPSS 16.0. Weight groups were determined by BMI reference values for German children as standardized by the German Obesity Association[155], defining BMI >90th percentile as overweight, >97th percentile as obese.

Normal distribution was tested using Kolmogorov-Smirnov-Test. Since the data show a Gaussian distribution, data are presented as mean and SD for continuous variables. Univariate, unadjusted analyses between obese and control subjects were performed with the independent samples t-test. ANCOVA was used to evaluate the presence of confounding variables in relationship between obesity status and vascular parameters. Models were adjusted for several confounding variables, including sex, age, height, systolic and diastolic blood pressure. Adjusted IMT means and 95% confidence interval (CI) were estimated with the use of Bonferroni method. Unadjusted relationships were assessed with Pearson's correlation analysis. To evaluate the independence of correlates of risk factors and to assess the main predictor for increased IMT, stepwise multiple linear regression analysis was used. IMT adjusted by sex and age was integrated in the model as dependent variable and BMI, the total percentage of body fat, systolic and diastolic blood pressure values were included as independent variables.

To evaluate the independence of correlations of IMT, cardiovascular risk factors and health- and skill-related physical fitness and to assess main predictors for increased IMT and cardiovascular risk factors, multiple linear regression analysis (enter method) was used. IMT, BMI, body fat, systolic and diastolic blood pressure (all adjusted by sex and age) were integrated as independent variables and the test components for health- and skill-related physical fitness were also adjusted by age and sex and integrated in the model as dependent variables.

In all regression analysis it was thoroughly checked for non-collinearity to avoid violations of model assumptions. Residuals were tested and the distribution was normal. All covariates included in the model were tested for interactions with each other. Because the variance inflation factor (VIF) was <5 and condition indices were <15 no correction for collinearity of the data was necessary [94]. A *P* value of less than 0.05 indicated statistical significance.

4.2.3 Results

Table 6 displays an overview of the anthropometric data and IMT of the A. carotis communis in overweight and obese patients compared to normal weight peers.

Table 6 Descriptive data of the studied obese patients compared to normal weight control subjects.

Values are presented as means +/- SD. Independent sample t-test was performed to investigate group differences. The level of significance was $P < 0.05$.

	Group	N	Mean	SD	*P* value
Age [years]	Normal weight	123	12.97	1.33	0.047
	Overweight/obese	89	13.39	1.68	
Height [m]	Normal weight	123	1.61	0.10	0.019
	Overweight/obese	89	1.64	0.09	
Weight [kg]	Normal weight	121	51.03	9.94	<0.001
	Overweight/obese	89	86.93	24.32	
BMI [kg/m^2]	Normal weight	123	19.31	2.03	<0.001
	Overweight/obese	89	31.76	6.96	
Body fat [%]	Normal weight	116	20.79	7.36	<0.001
	Overweight/obese	85	37.91	7.47	
Systolic blood pressure [mmHg]	Normal weight	122	111.87	11.08	<0.001
	Overweight/obese	85	122.56	14.37	
Diastolic blood pressure [mmHg]	Normal weight	122	67.38	9.06	0.002
	Overweight/obese	85	63.36	8.51	
IMT [mm]	Normal weight	91	0.532	0.045	0.023
	Overweight/obese	74	0.548	0.045	

In total, the obese and overweight patients were older (p=0.047). They were also significantly taller than their lean peers. Unquestionably the obese and overweight children and adolescents were significantly more weight, showed a higher BMI and a higher percentage of total body fat compared to the control group (all p<0.001). Systolic blood pressure was significantly (p<0.001) higher in overweight and obese children as well as diastolic blood pressure (p<0.001). The IMT was significantly (p=0.023) thicker in overweight and obese children compared to normal weight children.

Differences between boys and girls are presented in Table 7 and Table 8 for overweight and obese children as well as the normal weight children. The overweight and obese boys were significantly taller (p=0.003), heavier, have a higher BMI a higher percentage of body fat and a higher systolic and diastolic blood pressure (p=0.049). Also the IMT was significantly increased (p=0.033) compared to the control group. There was no significant difference in age (p=0.075) in boys.

Overweight and obese girls were heavier, showed a higher BMI, as well as a higher total percentage of body fat (all p<0.001). Further, systolic blood pressure (p<0.001) and diastolic blood pressure (p=0.011) were increased compared to the healthy control group in girls.

Concerning IMT in girls, no significant difference was found in overweight and obese subjects compared to the non-obese controls.

Table 7 Descriptive data of the studied obese patients compared to normal weight control subjects for boys.

Values are presented as means +/- SD. Independent sample t-test was performed to investigate group differences**.** The level of significance was *P* < 0.05.

		Group	N	Mean	SD	*P* value
Boys	Age [years]	Normal weight	67	13.01	1.38	0.075
		Overweight/obese	45	13.51	1.53	
	Height [m]	Normal weight	67	1.62	.11	0.003
		Overweight/obese	45	1.68	.09	
	Weight [kg]	Normal weight	67	51.85	11.13	<0.001
		Overweight/obese	45	90.81	25.26	
	BMI [kg/m^2]	Normal weight	67	19.46	2.08	<0.001
		Overweight/obese	45	31.67	6.22	
	Body fat [%]	Normal weight	62	17.48	8.14	<0.001
		Overweight/obese	43	36.56	8.06	
	Systolic blood pressure [mmHg]	Normal weight	67	113.48	11.15	<0.001
		Overweight/obese	45	124.00	15.58	
	Diastolic blood pressure [mmHg]	Normal weight	67	67.91	9.59	0.049
		Overweight/obese	45	64.31	9.04	
	IMT [mm]	Normal weight	53	.535	.045	0.033
		Overweight/obese	32	.555	.037	

Table 8 Descriptive data of the studied obese patients compared to normal weight control subjects for girls.

Values are presented as means +/- SD. Independent sample t-test was performed to investigate group differences**.** The level of significance was *P* < 0.05.

Sex		Group	N	Mean	SD	*P* value
Girls	Age [years]	Normal weight	56	12.92	1.29	0.289
		Overweight/obese	44	13.26	1.83	
	Height [m]	Normal weight	56	1.61	.08	0.889
		Overweight/obese	44	1.61	.08	
	Weight [kg]	Normal weight	56	50.05	8.27	<0.001
		Overweight/obese	44	82.97	22.92	
	BMI [kg/m^2]	Normal weight	56	19.14	1.96	<0.001
		Overweight/obese	44	31.86	7.70	
	Body fat [%]	Normal weight	54	24.59	3.72	<0.001
		Overweight/obese	42	39.30	6.61	
	Systolic blood pressure [mmHg]	Normal weight	56	109.91	10.78	<0.001
		Overweight/obese	40	120.95	12.87	
	Diastolic blood pressure [mmHg]	Normal weight	56	66.73	8.42	0.011
		Overweight/obese	40	62.30	7.85	
	IMT [mm]	Normal weight	38	.528	.046	0.174
		Overweight /obese	42	.543	.050	

The analysis of carotid IMT in the total study population revealed that, when adjusted for sex, age and height there was still evidence of statistically significant differences between obese children and adolescents and control subjects. IMT in overweight and obese patients was than 0.549 mm (95% CI 0.538 – 0.559) and in healthy control subjects it was 0.532 mm (95% CI 0.523 – 0.542, p=0.022). Adding diastolic blood pressure as a covariate reduced the p-value, but the statistical significance was retained (p=0.037). However, when systolic blood pressure was substituted the statistical significance was further reduced to a level that did not reach the formal level of statistical significance. IMT in obese patients was then 0.547 mm (95% CI 0.536 –

0.558), and IMT in healthy control subjects was 0.533 mm (95% CI 0.524 – 0.543, p=0.076).

Relationships between IMT and traditional cardiovascular risk factors in overweight and obese children and adolescents

The results of the unadjusted correlation analysis of anthropometric parameters, traditional cardiovascular risk factors (BMI, the total percentage of body fat, systolic and diastolic blood pressure) and IMT are presented in Table 9. Age was found positively correlated to IMT (r=0.213, p=0.041) as well as weight (r=0.225, p=0.032) and BMI (r=0.263, p=0.015).

In the multiple linear regression analysis BMI was shown to be the only predictor for variable (ß=0.263, p=0.030) for IMT (F [1.66] = 4.899, p=0.030), adjusted R^2 = 5.5%. However, after IMT was adjusted for sex and age the statistical significance reduced to a level that did not reach the formal level of significance (r=0.185, p=0.065).

Further BMI was positively related to systolic blood pressure (r=0.291, p=0.008). Moreover, the total percentage of body fat was related to systolic blood pressure (r=0.261, p=0.016).

Table 9 Relationships between non-invasive cardiovascular risk factors in overweight and obese patients (n=68).

Pearson correlation coefficients and *P* values are describing the relationship. The level of significance was defined as $P < 0.05$.
Abbreviations: IMT: Intima-media thickness of the A. carotis communis BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure;.

		IMT [mm]	Age [years]	Height [m]	Weight [kg]	BMI [kg/m^2]	Body fat [%]	SBP [mmHg]	DBP [mmHg]
IMT [mm]	r	1.000	0.213	0.062	0.225	0.263	0.184	0.173	-0.027
	P value	.	0.041	0.307	0.032	0.015	0.067	0.079	0.414
Age [years]	r	0.213	1.000	0.513	0.514	0.388	0.335	0.130	-0.131
	P value	0.041	.	0.000	0.000	0.001	0.003	0.146	0.143
Height [m]	r	0.062	0.513	1.000	0.718	0.330	0.309	.4002	0.126
	P value	0.307	0.000	.	0.000	0.003	0.005	0.000	0.153
Weight [kg]	r	0.225	0.514	0.718	1.000	0.885	0.644	0.402	0.070
	P value	0.32	0.000	0.000	.	0.000	0.000	0.000	0.286
BMI [kg/m^2]	r	0.263	0.388	0.330	0.885	1.000	0.726	0.291	0.030
	P value	0.015	0.001	0.003	0.000	.	0.000	0.008	0.406
Body fat [%]	r	0.184	0.335	0.309	0.644	0.726	1.000	0.261	-0.116
	P value	0.067	0.003	0.005	0.000	0.000	.	0.016	0.174
SBP [mmHg]	r	0.173	0.130	0.402	0.402	0.291	0.261	1.000	0.256
	P value	0.079	0.146	0.000	0.000	0.008	0.016	.	0.018
DBP [mmHg]	r	-0.027	-0.131	0.126	0.070	0.030	-0.116	0.256	1.000
	P value	0.414	0.143	0.153	0.286	0.406	0.174	0.018	.

Health-related and skill-related physical fitness

Table 10 presents the results of the health-related and skill-related physical fitness tests in overweight and obese boys compared to normal weight controls.

Table 10 Health- and skill-related physical fitness test results in overweight and obese boys compared to normal weight peers.

Pearson correlation coefficients and *P* values are describing the relationship. The level of significance was defined as $P < 0.05$.

	Group	N	Mean	SD	*P* value
Tapping [Hz]	Normal weight	67	11.04	1.34	<0.001
	Overweight/obese	45	15.58	9.33	
Drop jump [msec]	Normal weight	67	145.92	19.73	<0.001
	Overweight/obese	45	219.38	62.74	
Coordination run [sec]	Normal weight	67	6.04	0.76	0.002
	Overweight/obese	45	8.99	7.34	
Complex reaction test [sec]	Normal weight	67	21.59	3.25	0.045
	Overweight/obese	45	23.66	5.26	
Sit-and-reach [cm]	Normal weight	67	-.59	7.63	0.017
	Overweight/obese	45	-5.34	11.73	
9-minute run [m]	Normal weight	0	-	-	-
	Overweight/obese	45	1064.2	195.8	
Bent-arm hang [sec]	Normal weight	0	-	-	-
	Overweight/obese	45	1.35	2.45	
Sit-ups [n]	Normal weight	67	24.13	9.65	0.010
	Overweight/obese	45	19.38	7.60	

Obese and overweight boys show inferior physical fitness in coordination and speed in comparison to their normal weight peers. Further, coordination and visual reaction time, performed in the complex reaction test, are reduced in overweight and obese children and adolescents compared to the results of normal weight peers. Moreover, obese boys show less flexibility and less abdominal muscular endurance. They ran 1064.2 ± 195.8 m in the 9-minunte run. The obese and overweight boys managed to hold themselves in a bent-arm hang for a mean time of 1.35 ± 2.45 sec.

Overweight and obese girls performed less in tapping (speed of limb movement) and drop jumps (reactive strength) compared to their normal weight peers.

Further obese girls were slower in the 10 m coordination run and also slower in the complex reaction test. The obese girls further demonstrate impaired harmstring, gluteal and lower back muscle flexibility. They ran 1062.3 ± 170.7 meters in the 9-minute run and managed to hold themselves in the bent-arm hang for 1.32 ± 2.61 seconds.

Interestingly, overweight and obese girls presented better abdominal muscular endurance compared to their lean peers (Table 11).

Table 11 Health- and skill-related physical fitness tests in overweight and obese girls compared to normal weight peers.

	Group	N	Mean	SD	*P* value
Tapping [Hz]	Normal weight	56	10.41	1.81	0.002
	Overweight/obese	44	14.40	8.91	
Drop jump [msec]	Normal weight	56	150.41	24.80	<0.001
	Overweight/obese	44	207.97	52.88	
Coordination run [sec]	Normal weight	56	6.36	1.11	0.001
	Overweight/obese	44	7.10	0.92	
Complex reaction test [sec]	Normal weight	56	22.09	3.11	0.019
	Overweight/obese	44	24.76	5.82	
Sit-and-reach [cm]	Normal weight	56	6.87	8.58	0.001
	Overweight/obese	44	-.34	10.45	
9-minute run [m]	Normal weight	0	-	-	-
	Overweight/obese	44	1062.3	170.7	
Bent-arm hang [sec]	Normal weight	0	.	.	-
	Overweight/obese	44	1.32	2.61	
Sit-ups [n]	Normal weight	56	19.37	6.16	0.121
	Overweight/obese	44	21.98	8.37	

Relationships between IMT and health-related as well as skill-related fitness in overweight and obese children

In the multiple linear regression analysis all health- and skill-related physical fitness test results were adjusted by age and sex and put into the model (enter) for predictor analysis of IMT, which was also adjusted for age and sex. The regression model did not reach the formal level of significance for IMT_{adj} (F [1.44] = 0.219, p=0.952), adjusted R^2 = 0,2%. No significant relationships revealed between IMT_{adj} and the health- and skill-related physical fitness tests (all adjusted for age and sex): $tapping_{adj}$ (r=0.038, p=0.751); drop $jumps_{adj}$ (r=0.010, p=0.938); coordination run_{adj} (r=0.067, p=0.583); complex reaction $test_{adj}$ (r=0.276, p=0.173); $sit\text{-}and\text{-}reach_{adj}$ (r=-0.14, p=0.251); 9-minute-run$_{adj}$ (r=-0.056, p=0.716); bent-arm hang$_{adj}$ r=-0.107, p=0.417); sit ups$_{adj}$ (r=-0.42, p=0.730).

However, the results of the physical fitness tests correlate with body composition. A positive relationship revealed between the performed ground contact time in drop jumps$_{adj}$ and BMI (r=0.340, p=0.004). Further a positive relation could be assessed between the reaction time in the complex coordination and reaction test$_{adj}$ and BMI (r=0.313, p=0.03). Further a negative relation revealed between the component of flexibility (sit-and-reach test $_{adj}$) and BMI (r=-0.225, p=0.04). Furthermore the achieved running performance in the 9-minute-run$_{adj}$ negatively correlated to systolic blood pressure$_{adj}$ (r=-0.275, p=0.04).

4.2.4 Discussion

Vascular risk of overweight and obesity in children and adolescents

Although the most severe complications of overweight and obesity do not manifest until later in life, cardiovascular health consequences may already be evident at a young age[77]. Furthermore the period of adolescence has been described as a critical period for the development and expression of obesity-related comorbidities in boys and in girls[156,157].

Summarizing the results, the present study documented:

1. Carotid IMT was significantly increased in overweight and obese children and adolescents compared to healthy controls.
2. Significant correlations revealed between IMT and age; IMT and weight; IMT and BMI.
3. Impaired health-related and skill-related physical fitness in overweight and obese adolescents in most of the tested components (except abdominal endurance strength in girls, which was not impaired).
4. No significant correlations revealed between IMT and health- or skill-related fitness components
5. Significant correlations revealed between traditional cardiovascular risk factors and health- as well as skill-related physical fitness components.

Vascular status in overweight and obese adolescents and relationships to traditional cardiovascular risk factors

In both sexes, the measured IMT values for overweight and obese adolescents in the present study range between the 50th and 75th percentile for boys and for girls in age group 12/13 years[5]. The overweight and obese children show a significant larger IMT than the control group.

This result could also be stated in boys, however in girls, no significant differences for IMT in overweight and obese adolescents compared to normal weight peers were found. The apparent discrepancy within the present study could be due to the small sample size in girls (42 obese versus 38 controls).

The increased IMT in overweight and obese adolescents was accompanied by significantly higher values in body weight, body fat, systolic blood pressure and diastolic blood pressure. These facts still revealed when adjusting for sex.

Further the correlation of cardiovascular risk factors such as weight and BMI with IMT as well as BMI and body fat with systolic blood pressure suggests that obesity in adolescents represents a powerful determinant of early manifestations of atherosclerosis and affects structural properties of major vessels[158]. The effect of structural changes appears to be mediated, at least in parts, by BMI and systolic blood pressure.

The results of the present study further confirm findings of several studies that documented the association of hypertension and childhood overweight as well as obesity[159-162]. Furthermore, it has been stated that obese children have a tenfold greater risk of developing hypertension in young adults compared to non-obese children. This result is of notable concern since blood pressure values tend to track from adolescence into adulthood, and especially in those who are overweight or obese[163,164].

Health- and skill-related physical fitness in overweight and obese adolescents and the correlations to vascular structure (IMT) and cardiovascular risk factors

It is increasingly recognized that physical activity and exercise in children and adolescents is an essential component of healthy growth and development. The biological mechanisms linking exercise, physical fitness and health in children are multifactorial and of special interest since an emerging epidemic of pediatric obesity, type 2 diabetes and the metabolic syndrome[165-167].

Some authors found differences in fitness between obese and non-obese children, while others did not[168-170]. In the present study health-related and skill-related physical fitness components in obese compared to normal weight adolescents were impaired. The obese adolescents had mainly impaired performance on all tests requiring propulsion or lifting of the body mass, such as tapping, running coordination and bent-arm hang. Energy intake exceeding energy expenditure is stored in the body mainly as fat, but also in protein. Stored protein increases fat free and muscle mass[171]. Therefore, overweight and obese subjects usually have more muscle mass compared with normal weight individuals[172]. This is associated with better absolute muscle strength in adolescents[173]. But most of the functional tasks require the lifting of body weight. Relative muscle strength (muscle strength in relation to body mass) is may be the key component of muscle strength to comply in daily life[171] and not the absolute muscle strength.

These poorer performances are probably due to the fact that their excess body fat is an extra load and therefore has a negative influence on relative muscle strength and muscular endurance, that needs to be moved or hold during weight-bearing tasks[174]. This then leads to less performance in many tests such as drop jumps, tapping, 10-m coordination run and bent-arm hang.

Interestingly in overweight and obese girls the numbers of performed sit-ups did not differ significantly in comparison to normal weight peers. When comparing the results of the control group to German reference values[93] the test performance in sit-ups was only sufficient on a five grading scale (very good, good, normal, moderately disturbed and severely disturbed).

Obesity[103] and overweight[175] had a strong negative effect on endurance and upper body muscular strength and muscular endurance. The present study is in agreement with the above two studies and further underline results of Malina and coworkers[176] and Ara and colleagues[177].

Further the results of the correlation analysis reveal a positive association between anthropometric data and skill-related physical fitness. This can be demonstrated especially in drop jumps, testing the reactive strength of lower extremities and measuring the ground contact time. The contact time is positively associated to weight and BMI that underlines the above mentioned negative impact of body weight in weight lifting tasks[174].

The performed coordination skill was positively associated to BMI, which underlines a more impaired overall coordination and reaction in obese children. Furthermore, in the present study, the overweight and obese adolescents performed significantly slower in the complex coordination and reaction test. Wagner an co-workers[178] underlined the importance of developmental coordination in overweight and obese children in the context of human development. The authors reinforced that the data are of particular interest since developmental coordination and obesity both track with age. The results of their study made clear that obese show higher severe risk of developmental coordination disorder in comparison to normal weight adolescents. The complex coordination test in the present study focused more on the coordination and reaction time, demonstrating less coordinative skills of overweight children. Further D'Hondt and colleagues[179] also stated that BMI-related differences in motor coordination were more pronounced in older children (10-12 years) than to younger children (5-7 years).

The fact that excess body adiposity also increases the likelihood of poorer trunk fitness has been stated previously[180,181] and could also be demonstrated in this study, whereas a negative correlation between flexibility and BMI was assessed.

On the other hand in the present study cardiorespiratory endurance tested by the 9-minute run was negatively associated to systolic blood pressure. This result underlines published data of intervention studies that reported an effectively reduced blood pressure in overweight and obese children after an exercise intervention[182]. Further the present results are in line with reports of the Children and Adolescents Trail for Cardiovascular Health (CATCH) study[153]. Analysis of the CATCH trail demonstrated a greater number of cardiovascular risk factors in heavier children and a lower performance on 9-minute endurance run.

Boreham and co-workers[79] demonstrated that relationships between fatness and coronary risk factors were stronger than between fitness and cardiovascular risk factors in adolescents. Also in this study, no association between skill-related physical fitness and IMT could be stated.

In adults, overweight but fit adults have lower atherosclerotic cardiovascular risk than unfit lean persons[183]. However, at present, no data are available for children which confirms these observations[184].

4.2.5 Conclusions

The study underlines that vascular structure changes with increased body weight. It could be proven that an increased IMT is present in overweight and obese adolescents compared to normal weight controls. Further overweight and obese children demonstrated impaired health- and skill-related physical fitness in almost all tested components. Therefore the results emphasize the need of an early focus on skill-related fitness. A better motor fitness might encourage overweight and obese adolescents to more sport activity. This is even more important since physical fitness components are in correlation with traditional risk factors. However a correlation between vascular structure and physical fitness could not be stated in the present study. The awareness of the complex relationships emphasized with the fact that obesity in childhood and adolescence is an important risk factor for cardiovascular disease[185-188] as well as morbidity and mortality in later life [189-191] underline the importance of early prevention. The necessity becomes even more clearly with the continuing increase of overweight and obese children[132,192,193].

5 Intervention strategies in obese children

5.1 The importance of exercise

Atherosclerosis is a complex and multifactorial disease starting to develop in youth, especially in the presence of risk factors[194].

The main approach to reducing obesity-related cardiovascular risk is to reduce body weight. Previous studies in adults describe that a reduction of BMI of at least 1, over a period of one year leads to a lower rate of morbidity[195]. Although in children, the interpretation of studies focusing on the result of reducing BMI is difficult, since BMI increases in healthy normal weight children with increasing age[155,196].

In childhood and adolescents there are only few studies showing that weight reduction leads to improvement of the atherogenetic risk factor profile[197].

The present study focuses on the role of physical activity and exercise to increase physical sport motor fitness and its role in anatomic vascular wall structure changes to improve endothelial structure.

Research suggests that appropriate eating and exercise behaviors should be an integral part to any management strategy promoting cardiovascular prevention and preventing obesity[198,199]. Further, intervention studies have demonstrated the utility of physical activity and exercise to improve metabolic regulation after 3 weeks of daily exercise and low calorie diet[200].

Modules in intervention programs are multifactorial and multi-disciplinary and include both dietary and physical exercise and activity pattern. Little is known, however, about the overt or subclinical incidences of vascular structure changes in pediatric population and the impact of interventions on them.

5.1.1 Objectives

Therefore, the objectives of the present study were to assess, if a short-term stationary rehabilitation program has an effect on cardiovascular risk factors, including vascular structural changes and health-related as well as skill-related physical fitness components. It was hypothesized that a 4-week hospitalized multidisciplinary intervention reduced cardiovascular risk factors such as BMI, the total percentage of body fat, systolic and diastolic blood pressure, resting heart rate and IMT.

Further it was hypothesized that by the intervention, health- and skill-related physical fitness components improved resulting in better abdominal muscular endurance strength, upper trunk muscular endurance strength, reactive strength, speed, coordination, reaction time, cardiorespiratory endurance capacity and flexibility.

5.1.2 Methods

Eighty-five obese adolescents, who attended a hospitalized intervention at the rehabilitative Clinic Gaissach, Bad Tölz/Germany were consecutively examined at baseline and 4-weeks later. The inclusion criteria for participation in the trail were: age 11 to 15 years, no history of cardiovascular disease and no personal history of diabetes mellitus or impaired fastening glucose. Obesity was defined as a BMI > 97th percentile, using population specific data[155]. All patients participated in the intervention according to the National guidelines[201]. The program was multi-disciplinary and based on physical exercise, nutrition education (high carbohydrate, fat reduced diet), and behavior therapy including individual psychological care of the child. An interdisciplinary team of pediatric medical doctors, diet assistance, psychologist and sport scientists were responsible of the interventional training.

The medical examination including anthropometric data collection and carotid IMT sonography was performed as previously described[5] at baseline and 4 weeks later. Respectively one day later the health- and skill-related physical fitness test was conducted. The fitness test included the following items and were conducted as described in chapter 4.2.4: Tapping (speed of limb movement)[146,147], drop jumps (reactive strength)[148], 10 meter coordination run (coordination and speed)[145,149], complex reaction test (coordination and reaction time)[145,150], sit-and-reach test (harmstring, gluteal and lower back muscle flexibility)[86], 9-minute run (cardiorespiratory endurance)[152,153], bent-arm hang (upper trunk muscular endurance strength)[86] and sit-ups (abdominal muscular endurance strength)[86,151,154].

Statistical analysis

Statistical analysis was performed using SPSS 17.0. Depending on the results of the Kolmogorov-Smirnov test, all continuous data are presented as mean ± standard deviation (SD). Comparisons were made between baseline and post examination 4-

weeks later and therefore the paired sample *t*-test for paired samples was used. A *P* value < 0.05 was considered to be significant.

5.1.3 Results

Effects of the hospitalized intervention

Table 12 presents an overview of the medical data at baseline and 4 weeks later. Anthropometric measurements revealed significant decrease in weight, BMI, and the total percentage of body fat. After the intervention the systolic blood pressure and diastolic blood pressure were significantly decreased. Further the heart rate decreased significantly. After 4 weeks the IMT did not change significantly.

Table 12 Changes in weight, BMI body composition, blood pressure heart rate and carotid IMT at baseline and 4 weeks after the hospitalized intervention.

	N	Baseline	SD	4-weeks later	SD	*P* value
Weight [kg]	85	91.44	22.93	82.52	20.65	<0.001
BMI [kg/m^2]	85	33.52	6.99	30.25	6.35	<0.001
Body fat [%]	85	40.18	5.49	36.17	6.34	<0.001
Systolic blood pressure [mmHg]	85	123.55	14.10	115.09	11.73	<0.001
Diastolic blood pressure [mmHg]	85	64.51	8.61	61.69	7.58	0.037
Heart rate [beats/min]	85	85.43	12.37	70.68	12.08	<0.001
IMT [mm]	85	0.549	0.041	0.543	0.050	0.440

Data presented as mean +/-SD. A *P* value ≤ 0.05 was considered to be significant.

Results in physical fitness revealed in most tests an increase in performance (Table 13). The tapping frequency significantly improved after 4 weeks. The ground contact time assessed by drop jumps also reduced significantly. The complex reaction test revealed a significant better overall coordination, resulting in a faster reaction time. Harmstring, gluteal and lower back muscle flexibility and cardiorespiratory endurance increased significantly after the 4-week intervention. The running coordination and speed assessed by the coordination run, upper body muscular endurance assessed by bent-arm hang and the abdominal muscular endurance assessed by sit-ups did not improve significantly.

Table 13 Changes in health- and skill-related physical fitness at baseline and 4 weeks after the hospitalized intervention.

	N	Baseline	SD	4-weeks later	SD	*P* value
Tapping [Hz]	85	16.41	9.89	9.67	1.45	<0.001
Drop Jump [msec]	85	229.31	60.33	205.18	50.76	0.011
Coordination run [sec]	85	8.64	6.71	7.04	1.37	0.121
Complex reaction test [sec]	85	27.67	5.60	21.26	2.77	<0.001
Sit-and-reach [cm]	85	-4.11	12.61	-1.40	8.65	0.048
9-minute run [m]	85	1084.5	150.7	1240.2	195.8	<0.001
Bent-arm hang [sec]	85	1.46	2.42	1.74	4.11	0.519
Sit-ups [n]	85	37.6	8.16	38.00	8.28	0.781

Data presented as mean +/-SD. A *P* value ≤ 0.05 was considered to be significant.

5.1.4 Discussion

The sedentary lifestyle and within that the imbalance of energy intake and expenditure contributes to the increased obesity prevalence in adolescents. Intervention strategies are multi-disciplinary, including nutritional, exercise and behavioral treatment programs.

The main finding of the study is that a 4-week hospitalized intervention already accounts for a significant reduction of atherosclerotic cardiovascular risk factors such as weight, BMI, the total percentage of body fat, systolic and diastolic blood pressure. These results are in line with previous pediatric intervention studies that demonstrated an improvement of cardiovascular risk factor profile in association with obesity[202-205].

In this context, studies of Meyer and colleagues[59] underlined that cardiovascular fitness plays an important role for the improvement of cardiovascular risk factors and further in cardiovascular health prevention to reverse any atherosclerotic damage.

It is further conceivable that exercise training improves endothelial function by its positive impact on traditional risk factors[55].

However, in the present study vascular structure (IMT) did not change significantly after 4-weeks of hospitalized intervention. This result is in line with reports of Woo and co-workers[206] who did not find changes in IMT after 6 weeks of exercise and diet intervention. It is possible that pathological changes need longer time for their adaptation of in this case re-adaptation.

Studies of Wunsch and colleagues[96] described parallel to an improvement of the cardiovascular risk profile with substantial weight loss, a decrease of IMT after a 1-year outpatient intervention program.

Taking traditional non-invasively measured cardiovascular risk factors into account the intervention program revealed a significant reduction of systolic and diastolic blood pressure. Those positive effects of exercise had been previously stated after a 8-months intervention program by McMurray and colleagues[207]. Richter and co-workers[208] explained the reduction of blood pressure firstly due to the enhancement of insulin action and glucose transport by physical exercise. A second explanation could be that the increased capitalization results in increased blood flow and energy supply to muscle tissue, which results in an improved fat metabolism and decreased blood pressure[208-211].

Advances in health- an skill-related physical fitness

Exercise training was a major component in the intervention, daily activity indoor and outdoor sport programs. The exercise intervention not only improved measures of cardiovascular risk factors, but also improved health-related and skill-related physical fitness. A significant improvement revealed in speed of lower limbs assessed by tapping, reactive strength assessed by drop jumps, complex coordination and reaction test, harmstring, gluteal and lower back muscle flexibility assessed by the sit-and reach test and in cardiorespiratory endurance which was assessed by the 9-minute run.

Complex health-related and skill-related physical fitness assessments in hospitalized intervention obese children are still rare. Results of a Belgium hospitalized intervention study[212] underlined the importance of coordination and motor skill development in overweight and obese children. Their results demonstrated impaired scores for overweight and obese children and an increase in test scores of the Körperkoordinationstest after a short-term intervention. The authors emphasized the importance of gross motor skills in obese children with regard to a possible increase in physical activity. Sola and colleagues[213] also tested a variety of different basic motor abilities and complex movements in different muscle groups before and after 6 and 12 months of intervention. They stated an improvement in physical fitness and also a reduction of BMI over the intervention time.

Eliakim and colleagues[143] described a significant increase in endurance capacity after a 3 months intervention including twice a week 1 hour of instructed training and additional self-administered physical activity tasks such as running or walking for at least 30 to 45 minutes per week.

5.1.5 Conclusions

The alterations of the analyzed cardiovascular risk factors were significantly related to the loss of weight throughout the intervention program. In advantage to invasive diagnostics, the ultrasound measurement can demonstrate the effect of the intervention program on the level of the vascular system since it enables an insight to the health of the blood vessel. No significant reduction of IMT could be measured after 4-weeks of hospitalized intervention. Obviously pathological changes need longer time to be reduced.

The multidisciplinary intervention with a focus on daily physical exercise revealed an enhancement in speed of lower limbs, reactive strength, complex coordination and reaction time, harmstring, gluteal and lower back muscle flexibility and endurance capacity. These positive effects might be beneficial for long-term physical activity and sport motor skill improvement.

6 *Obesity prevention in school-settings*

6.1 Introduction

The prevalence of overweight and obesity is increasing in Western societies. Data from the German National Health Survey (2003 - 2006) describe that in Germany 15% (1.9 million) of the 3-17 year old children are overweight and thereof 6.3% (800.000) are obese. Comparing those numbers to reference values from 1985-1999 the frequency of overweight occurrence has increased by 50% and the obesity rate has doubled[214].

Data of the Bavarian school entrance examinations demonstrate an increase of overweight children from 8.5% in 1992 to 12.3% in 1997 as well as an increase of obese children from 1.8% in 1992 to 2.8% in 1997[215]. Looking at the data of the school entrance examination for the year 2006/07 8.8% of the children were overweight (8.7% of the girls and 8.9 % of the boys). Furthermore the number of obese children increased to a total of 3.5% (3.3% of the girls and 3.7% of the boys)[216].

The reasons for an increased obesity rate are multifactorial. Next to familiar predispositions a disparity between energy intake and energy expenditure is relevant. Furthermore, the school as learning institution itself as well as parent's lifestyle and the reduction of leisure time physical activity are pertinent[217]. Beside sport clubs, schools further influence children's level of physical activity.

In Bavaria, schools have a high quality of physical education classes with a minimum of 3 times per week to a total of 135min/week which is compulsory by law. Those school-based physical education programs help children to remain physical active. However, physical education classes are often under-evaluated despite their importance in achieving fitness, skills and health. In addition to physical education classes, special school programs like "Die bewegte Schule" ("The moving school") are supposed to increase physical activity in other subjects outside physical education. The idea behind is that the release of energy and stress may also help children to more cognitive concentration in the classroom[218].

To promote physical activity in schools, making it part of the curriculum and implementing activity outside physical education classes is relevant, since it has been described that sport motor fitness abilities are reduced[219]. The authors point out that the promotion of physical education would motivate the school children to more activity.

The fact that more activity has a positive impact on body weight has been described by Zoroli and co-workers[220] who compared sport intensive classes to control classes. The sport intensive classes showed less overweight children than the controls. Especially in the context of school careers, results of Graf and coworkers[221] are also important. They found out that sport motor ability "coordination" correlates with cognition tests. Additionally a meta-analysis of 134 studies including reaction tests and complex mental combination tasks demonstrated that cognitive performance significantly (p=0.025) increased with physical activity[222]. Short-term activity programs weren't as successful as long-term physical activity and health programs.

In addition to schools and sport clubs, governments can provide opportunities to implement obesity prevention programs though after school programs. In 2004 the Bavarian Ministry of Environment and Public Health launched a health initiative: „Gesund. Leben. Bayern" ("Healthy. Living. Bavaria").

In this health promotion initiative the physical activity school program „Sport past 1 o´clock" affiliates regional sport clubs and schools for better networking and combines resources, with the main aim to increase children's physical activity and long-term affiliation to a local sport club. Such a network was set up in Germering, where the local sport club SV Germering started a physical activity program, offering Basketball training for primary school children, after school.

6.1.1 Objectives

The main objectives of this pilot study were to determine the effect of a school basketball program, without a dietary intervention, on body composition, health-and skill-related physical fitness and non-invasively measured cardiovascular risk factors.

It was hypothesized that a 90 min Basketball intervention program revealed in a reduction of BMI and total percentage of body fat, a reduction in systolic and diastolic blood pressure and a reduction in IMT compared to the control group. Further it was assumed that the basketball training revealed an increase in health-related and skill-related performance, compared to the control group.

6.1.2 Methods

The SV Germering contacted the Institute of Public Health Research (now Institute of Preventive Pediatrics) of the Technische Universität München with the inquiry to evaluate the existing basketball program. A research proposal was successfully submitted to the Bavarian Ministry of Environment and Public Health. The Ministry supported the evaluation for a study period of one year within the framework of the health and physical activity initiative “Sport past 1 o’clock”.

Children were recruited from all four primary schools in Germering. The project was introduced via parents’ information evenings in the schools in December 2004. Leaflets for children underlined the information given to the parents.

In order to test whether the 6-months basketball training improves cardiovascular risk factors all children in the intervention group were tested for BMI, the total percentage of body fat, systolic blood pressure, diastolic blood pressure, resting heart rate and IMT, harmstring, gluteal and lower back muscle flexibility (sit- and-reach test), anaerobic cardiorespiratory endurance (step test), upper trunk muscular endurance strength (bent-arm hang), abdominal muscular endurance strength (sit-ups), speed of limb movements (tapping), reactive strength (drop jumps), acceleration and speed (20 meter run), coordination and visual reaction time (simple reaction test), coordination and speed (complex reaction test). They further undertook a basketball intervention program, and were then examined again at the end of the program, 6 months later.

The children of the control group were also examined at baseline, had no specific training and were then tested after 6 months. They performed the same tests as the children of the intervention group as stated above and also the same testing times.

The entrance examination took part on 22nd and 23rd of January 2005 in the sports gymnasium at Kleinfeldstrasse in Germering, followed by a final examination on 2nd and 3rd July 2005. The intervention consisted of 6-months basketball training (90 min per week). The intervention was set up and conducted in close cooperation with the local sports club SV Germering and was also held in the sports gymnasium at Kleinfeldstrasse, easy to access for all children of the intervention group.

Sixty-four primary school children took part in the baseline and post examination 6 months later. The children were divided in 6 groups and performed the physical fitness tests as well as the medical diagnostics in a standardized routine. The medical examination took part before the children entered the sports hall for their physical fitness tests.

Since it was a requested evaluation of an existing program, 12 children had already participated in the basketball-training group and therefore stayed in the intervention group. 8 children were randomly selected from the participants at baseline. In total n=20 Children took part in the basketball intervention

Before the examination all participating children turned in their written informed consensus for participation, signed by their legal representative. The study was approved by the Ethics Committee of the Faculty of Medicine, Technische Universität München (protocol number 1162/04).

Medical examination and physical fitness test battery

The anthropometrical data collection (weight, height, body mass index, total percentage of body fat, systolic and diastolic blood pressure as well as the sonography of the A. carotis communis, measuring the intima-media thickness (IMT) were performed as previously reported by Böhm and colleagues[5].

Health-related and skill-related physical fitness test

To assess health-related and skill-related components of physical fitness all subjects performed valid and reliable tests from standardized test batteries. The physical fitness test was adjusted to subject’s age and conducted in a school gymnasium, provided with standard gymnastic facilities. After a standardized 10-minute warm-up program the tests were performed in a defined order. The objective for the composition of the used fitness test battery was to analyze a multitude of different components of health-related and skill-related physical fitness such as anaerobic cardiorespiratory endurance, muscular strength and muscle endurance, speed, coordination, reaction time and harmstring, gluteal and lower back muscle flexibility. The tests were chosen because of the ease of their administration to large numbers of subjects and its choice of reliable and valid fitness measures for a general healthy pediatric population.

The participants received verbal encouragement from the investigators to achieve maximum performance. The physical fitness tests were performed at five tests stations. At each test station two trained staff members supervised and conducted the examination.

Test station I included “20-m run” and “10-m coordination run”, examining acceleration from 0-10 meters as well as speed and running coordination. Test station II included complex and simple reaction tests, analyzing coordination and visual reaction time. Test station III, included the tests “tapping”, examining speed of limb movement and “drop jump” to test reactive strength. At test station IV the harmstring, gluteal and lower back muscle flexibility test “sit-and-reach” as well as a “step test” to measure anaerobic endurance capacity was conducted. Test station V included two muscular endurance tests, the “bent-arm hang” to test upper trunk muscular endurance and “sit-ups” to test abdominal muscular endurance.

A brief description of the physical fitness test battery follows below:

Sit-and-reach – assessment of harmstring, gluteal and lower back muscle

The sit-and-reach test was performed as previously described in Chapter 3.3.2[86,87]

Step test – assessment of anaerobic cardiorespiratory endurance

The test measures the cardiorespiratory endurance. The test person steps up (both knees stretched on top) on a normal gymnastic bench in a given velocity, about 40 times per minute. A metronome is preset for the test person to help him/her following the right step velocity. Pulsoxymeters are used to measure the heartbeats during the test and during the recovery time.

At the beginning of the test the resting heart rate is measured after 5 min in a sitting position. Right after the test the max heart rate is measured. The recovery pulse rate is taken 2 min after the endurance test in a sitting position. The test value is taken from the difference of the resting and recovery pulse rate. The measured data from resting hear rate, maximal heart rate und recovery heart rate as well as the performed steps on the bench were transformed to age and sex specific t-values Each test person performs one trail of the endurance test[223,224].

Bent-arm hang - assessment of upper trunk muscular endurance

The bent-arm hang test was performed as previously described in Chapter 3.3.2[86].

Sit-ups - assessment of abdominal muscular endurance strength

The number of sit-ups was tested as previously described in Chapter 3.3.[85]

Tapping – assessment of speed of limb movement

The tapping test was performed as previously described in chapter 4.2.4[146,147].

Drop jump - assessment of reactive strength

The drop jump test was performed as previously described in chapter 4.2.4[148]

20-meter run (acceleration 0-10 meters and speed 10-20 meters)

The aim of the test is to run 20 meters as fast as possible. The time is counted via light barriers. The examiner starts the set up and the time is counted as soon as the test person runs through the first light barrier. An intermediate time is measured after 10 meters. Therefore the following components can be tested: 0-10 meters acceleration and 10 - 20 meters running speed. Each subject has three trails. The fasted run is counted for further analysis[147,149].

Coordination run - assessment of speed and coordination

To assess speed and running coordination the 10m coordination run was performed as previously described in chapter 4.2.4.[145,149]

Simple reaction test - assessment of visual reaction time

On the computer screen visual red squares appear after a random time between 2 to 4 seconds on a black background. The aim is, to touch the hand sensor plate as fast as possible after the recognition of the visual sign. Measured is the reaction time in milliseconds [msec]. As a start position the test person is holding his/her hand next the body and moves it back to that position after each reaction move. The test serial consisted of 10 visual signs. The two fastest and slowest reactions are deleted from the trail serial. From the 6 remaining values the mean is counted and used for further analysis[145].

Complex reaction test – assessment of coordination and reaction time

To assess coordination and reaction time an complex reaction test was performed as previously described in chapter 4.2.4[145,150].

The intervention program

The intervention program consisted of 90 minutes basketball training per week organized and held by a nationally certified and experienced basketball coach of the SV Germering. The first 10 minutes were free exercise time for the children. They were allowed to dribble, throw on the baskets getting familiar with the ball with the main aim of „getting ready for the class“. This phase was followed by a 20 minutes supervised warm up with coordination exercise, ball handling, balance training and coordination runs with and without the basketball. Afterwards technical training with throwing, dribbling and shooting was followed for 30 minutes. The next 30 minutes consisted of a basketball game “five against five players”. To assure a game and a high running amount rules were simplified. The main aim was to guarantee changes of directions and changes of running speed during long running periods. The basketball training was conducted in the style of training recommendations of the German Basketball Federation for school children and basketball club training.[225] [226,227]

Statistical analysis

Data were encoded, checked and subsequently analyzed using SPSS 17.0. Weight groups were determined by age- and gender-specific BMI reference values for German children as standardized by the German Obesity Association[155], defining BMI < 10^{th} percentile as underweight, ≥10 to <90^{th} percentile as normal BMI ≥90^{th} percentile as overweight, ≥97^{th} percentile as obese. Hypertension was defined with regard to sex and age by values above the 95^{th} percentile of the International Task Force[92]. IMT values were classified into three groups following German sex- and age-specific reference values[5]: < 25^{th} percentile, ≥ 25^{th} to <75^{th} percentile and values > 75^{th} percentile. Normal distribution was tested using Kolmogorov-Smirnov Test.

Levene's test for equality of variances was calculated to test that the conditions of the samples are equal. Univariate analysis of variance was tested to evaluate differences between means of various groupings of a single dependent variable. If the assumption of homogeneity of variance was violated, the Welch *F* – ratio was reported.

To identify differences between baseline (pre-test) and after the intervention (post-test) Student's dependent *t* - test for paired samples were calculated.

A *P* value ≤ 0.05 was considered statistically significant.

6.1.3 Results

A total of n=64 children took part in the pre-test at baseline and post examination after the intervention. Thereof, 19 children belong to the intervention group and 45 children to the control group. The Kolmogorov-Smirnov Test revealed that all variables were normally distributed, therefore data are presented as means ± SD. Table 14 and 15 present mean values ± SD of anthropometrical data and cardiovascular risk factors for boys and girls. At baseline no significant differences in anthropometrical data and cardiovascular risk factors existed between the intervention and the control group either in boys no in girls.

Table 14 Anthropometric data and cardiovascular risk factors in boys at baseline.

(Independent Students t-test for group comparison. The significance level is $P \leq 0.05$).

	Group	N	Mean	SD	*P* value
Age [years]	Control subjects	23	8.9	0.3	0.923
	Intervention group	7	8.9	0.5	
Weight [kg]	Control subjects	23	31.3	6.1	0.931
	Intervention group	7	32.3	5.9	
Height [m]	Control subjects	23	1.37	0.7	0.982
	Intervention group	7	1.37	0.6	
BMI [kg/m^2]	Control subjects	23	16.66	2.66	0.942
	Intervention group	7	16.74	1.97	
Body fat [%]	Control subjects	23	23.03	3.01	0.758
	Intervention group	7	23.41	2.11	
Systolic blood pressure [mmHg]	Control subjects	23	101.52	8.84	0.981
	Intervention group	7	101.43	8.99	
Diastolic blood pressure [mmHg]	Control subjects	23	67.17	8.89	0.208
	Intervention group	7	72.14	9.06	
Heart rate [beats/min]	Control subjects	22	93.18	11.39	0.213
	Intervention group	7	86.57	13.69	
IMT mean [mm]	Control subjects	11	0.502	0.044	0.347
	Intervention group	5	0.480	0.038	

Table 15 Anthropometric data and cardiovascular risk factors in girls at baseline.

(Independent Students t-test, for group comparison. The significance level is $P \leq 0.05$).

	Group	N	Mean	SD	*P* value
Age [years]	Control subjects	22	8.8	0.6	0.941
	Intervention group	12	8.8	0.4	
Height [m]	Control subjects	22	1.37	0.7	0.935
	Intervention group	12	1.36	0.6	
Weight [kg]	Control subjects	22	32.5	6.6	0.201
	Intervention group	12	30.6	4.9	
BMI [kg/m^2]	Control subjects	22	16.04	1.36	0.126
	Intervention group	12	17.05	2.39	
Body fat [%]	Control subjects	22	18.13	2.02	0.071
	Intervention group	12	19.56	2.31	
Systolic blood pressure [mmHG]	Control subjects	22	100.23	7.63	0.331
	Intervention group	12	103.18	9.02	
Diastolic blood pressure [mmHG]	Control subjects	22	66.14	7.70	0.497
	Intervention group	12	68.18	8.73	
Heart rate [beats/min]	Control subjects	22	89.43	11.43	0.323
	Intervention group	12	93.60	9.22	
IMT [mm]	Control subjects	15	0.485	.048	0.140
	Intervention group	5	0.529	.073	

Table 16 Levene's test for equality of variances at baseline

Variable	***F* [df 1, 2]**	***P* value**
BMI [kg/m^2]	1.905 [df 3, 60]	0.138
Body fat [%]	0.669 [df 3, 60]	0.574
Systolic blood pressure [mmHg]	1.585 [df 3, 60]	0.202
Diastolic blood pressure [mmHg]	0.374 [df 3, 60]	0.772
Heat rate [mmHg]	0.1092 [df 3, 60]	0.360
IMT [mm]	1.863 [df 3, 32]	0.156
The results of the homogeneity test revealed that the null hypothesis – the variances of the dependent variables are equal across groups - can be retrained for all variables.		

Sex differences between intervention and control group were analyzed and baseline.

Table 17 displays differences in medical parameters between boys and girls for each group at baseline. In the control (p<0.001) and intervention group (p=0.002) we could demonstrate that the total percentage of body fat was significantly higher in boys compared to girls. All other cardiovascular parameters such as BMI, systolic blood pressure, diastolic blood pressure, resting heart rate and IMT do not differ significantly between boys and girls.

Table 17 Sex differences for cardiovascular parameters between the intervention and control group at baseline.

(Independent sample Mann-Whitney U Test. The significance level is $P \leq 0.05$).

Group		Sex	N	Mean	SD	*P* value
Controls	BMI [kg/m^2]	Boys	23	16.65	2.66	0.335
		Girls	22	16.03	1.36	
	Body fat [%]	Boys	23	23.03	3.01	<0.001
		Girls	22	18.13	2.02	
	Systolic blood pressure [mmHg]	Boys	23	101.52	8.84	0.603
		Girls	22	100.23	7.63	
	Diastolic blood pressure [mmHg]	Boys	23	67.17	8.89	0.678
		Girls	22	66.14	7.70	
	Heart rate [beats/min]	Boys	23	93.18	11.39	0.278
		Girls	22	89.43	11.43	
	IMT [mm]	Boys	11	0.502	0.044	0.360
		Girls	15	0.485	0.048	

Continuation of Table 17

Intervention group	BMI [kg/m^2]	Boys	7	16.73	1.97	0.778
		Girls	12	17.04	2.39	
	Body fat [%]	Boys	7	23.41	2.11	0.002
		Girls	12	19.56	2.31	
	Systolic blood pressure [mmHg]	Boys	7	101.43	8.99	0.693
		Girls	12	103.18	9.02	
	Diastolic blood pressure [mmHg]	Boys	7	72.14	9.06	0.369
		Girls	12	68.18	8.73	
	Heart rate [beats/min]	Boys	7	86.57	13.69	
		Girls	12	93.60	9.22	0.223
	IMT [mm]	Boys	5	0.480	0.038	0.224
		Girls	5	0.529	0.073	

Boys had a significantly higher total percentage of body fat than girls (Table 17). However, at baseline the factors sex (male; female) and the group affiliation (control and intervention group) had no effect on BMI, systolic blood pressure, diastolic blood pressure, heart rate and IMT (Table 18). Results of the ANOVA revealed that sex had an effect on the total percentage of body fat, F=39.12 [df 3, 60], $p<0.001$; $r^2 = 0.395$, 39.5% (Table 18).

Table 18 Results of the univariate analysis of variance to test effects of sex and group affiliation on cardiovascular risk factors at baseline.

Dependent variable	Fixed factors	*F* [df 1, 2]	*P* value
BMI [kg/m^2]	Sex (male; female)	0.065 [df 3, 60]	0.799
	Group (intervention; control group	0.800 [df 3, 60]	0.375
Body fat [%]	Sex (male; female)	39.21 [df 3, 60]	<0.001*
	Group (intervention; control group	1.675 [df 3, 60]	0.201
Systolic blood pressure [mmHg]	Sex (male; female)	0.009 [df 3, 60]	0.924
	Group (intervention; control group	0.353 [df 3, 60]	0.555
Diastolic blood pressure [mmHg]	Sex (male; female)	1.076 [df 3, 60]	0.304
	Group (intervention; control group	2.119 [df 3, 60]	0.151
Heat rate [mmHg]	Sex (male; female)	0.247 [df 3, 60]	0.621
	Group (intervention; control group	0.137 [df 3, 60]	0.713
IMT [mm]	Sex (male; female)	0.715 [df 3, 32]	0.404
	Group (intervention; control group	0.326 [df 3, 32]	0.572

Effect of the intervention program on cardiovascular risk factors

Body mass index

The main aim of the study was to evaluate the effect of 6-months basketball training on cardiovascular risk factors. Neither in the intervention nor in the control group significant difference of BMI at baseline and 6 months later could be assessed. In the intervention group the BMI slightly increased from 16.93 ± 2.20 kg/m^2 to 17.27 ± 2.16 kg/m^2, but the increase was not significant, $t\,[18] = -1.775$, $P = 0.093$.

In the control group the BMI slightly increased by 0.19 ± 0.06 kg/m^2 from 16.35 ± 2.12 kg/m^2 to 16.54 ± 2.18 kg/m^2 in the control group, but the increase was also not significant, $t\,[44] = -1.965$, $P = 0.056$ (Figure 5).

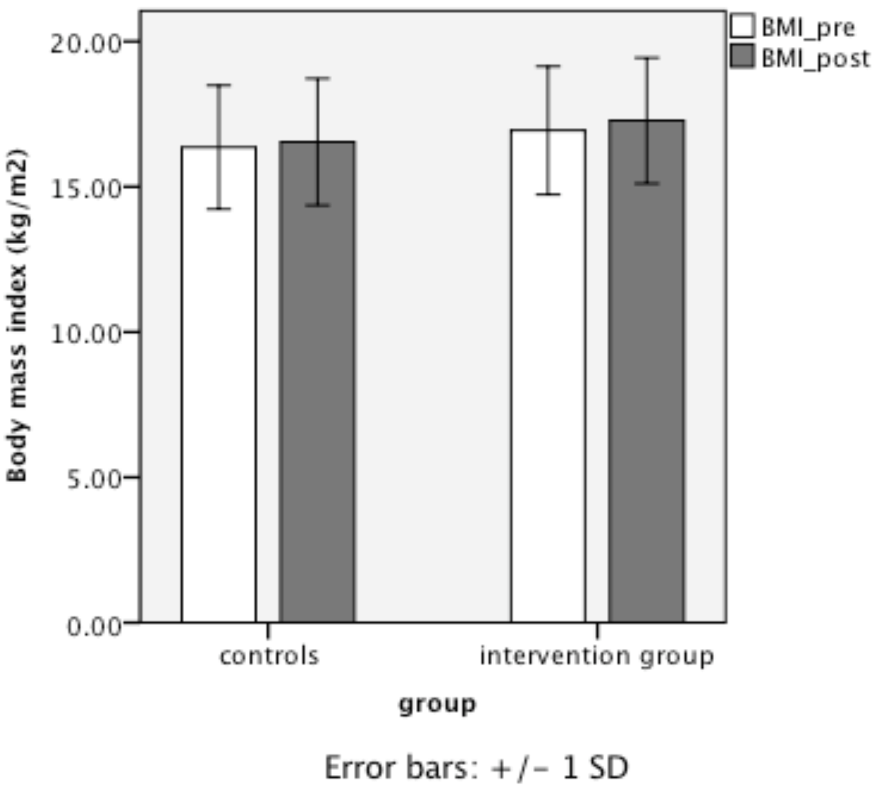

Figure 5 Development of the body mass index from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: $P < 0.05$*; $P < 0.01$**; $P < 0.001$***).

The total percentage of body fat

The total percentage of body fat significantly (t [15] = -2.890, P = 0.011) increased by 0.96 ± 0.08 % from 21.12 ± 3.03% to 22.08 ± 2.95% in the intervention group.

Similarly the total percentage of body fat significantly (t [44] = -4.758, P <0.001) increased in the control group from 20.63 ± 3.55 % to 21.47 ± 3.59 % (Figure 6).

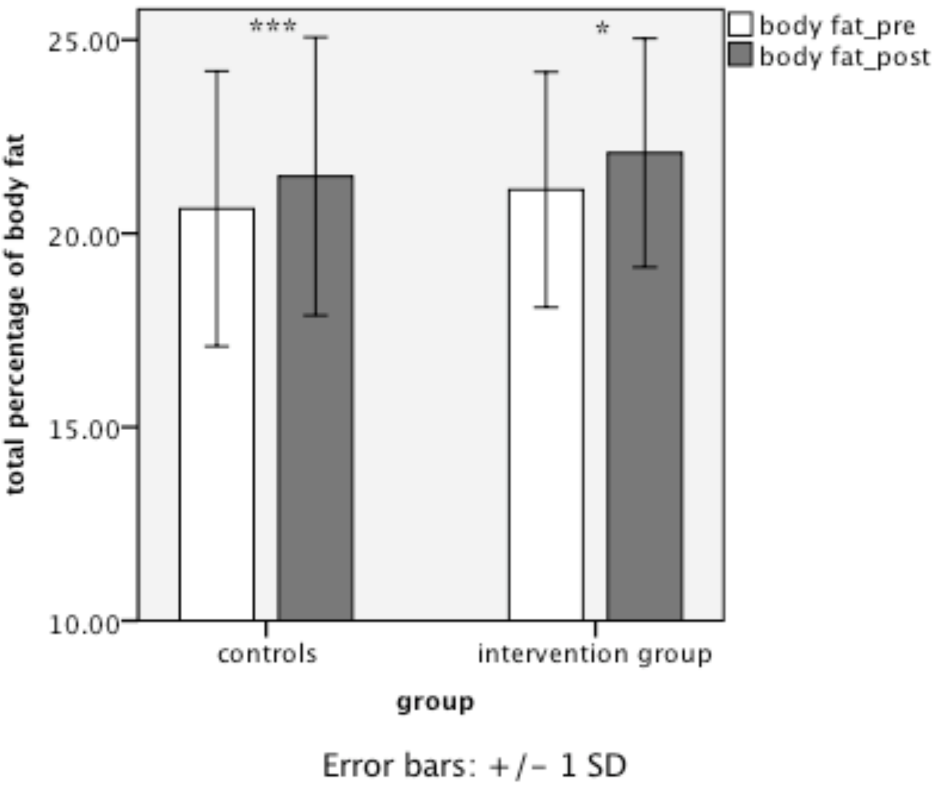

Figure 6 Development of the total percentage of body fat from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: P < 0.05*; P < 0.01**; P < 0.001***).

Systolic blood pressure

After the six months basketball training systolic blood pressure significantly increased in the intervention group. At baseline the mean systolic blood pressure was 102.50 ± 8.78 mmHg and after 6 months it increased significantly ($t\,[17] = -2.758$, $P = 0.013$) to 106.94 ± 6.21 mmHg. In the control group the systolic blood pressure slightly increased from 100.89 ± 8.20 mmHg to 102.00 ± 6.69 mmHg. The increase was not significant, $t\,[44] = -0.797$, $P = 0.430$ (Figure 7).

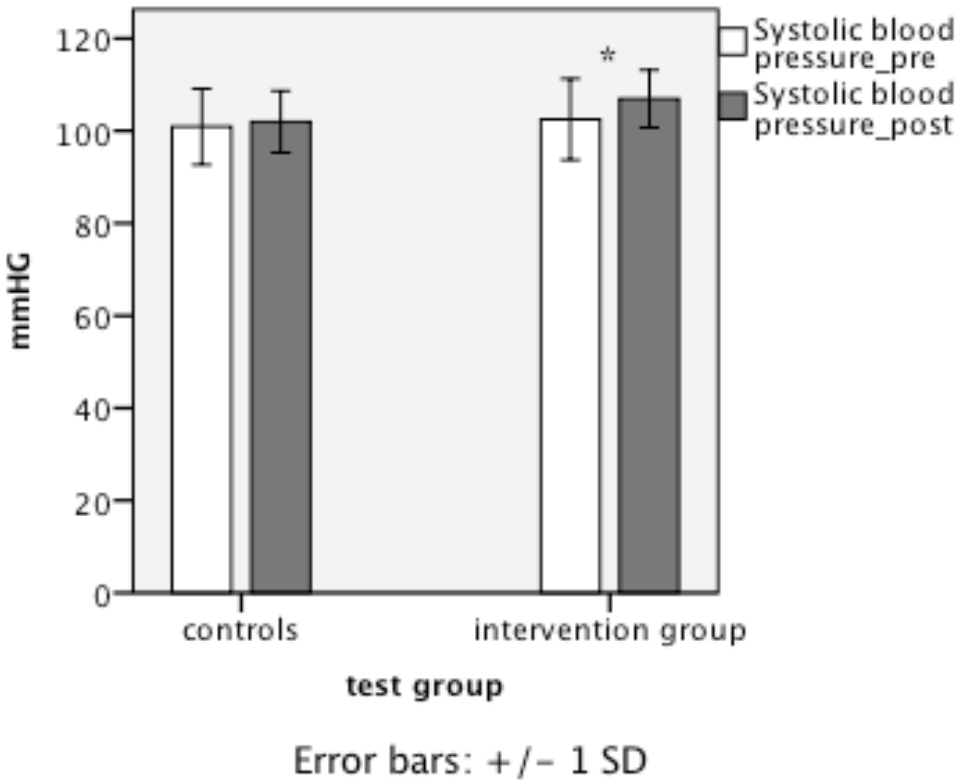

Figure 7 Development of the systolic blood pressure from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: $P < 0.05$*; $P < 0.01$**; $P < 0.001$***).

Diastolic blood pressure

There were no significant differences in diastolic blood pressure between baseline and 6 months later. This was the fact either with basketball training (intervention group) or without training (controls). The diastolic blood pressure reduced from 69.72 ± 8.82 mmHg to 66.39 ± 6.37 mmHg; *t* [17] = 1.617, *P* = 0.124 in the intervention group. In the control group the reduction was from 66.67 ± 8.25 mmHg to 65.33 ± 6.77 mmHg; *t* ([44] = 1.259, *P* = 0.215) (Figure. 8).

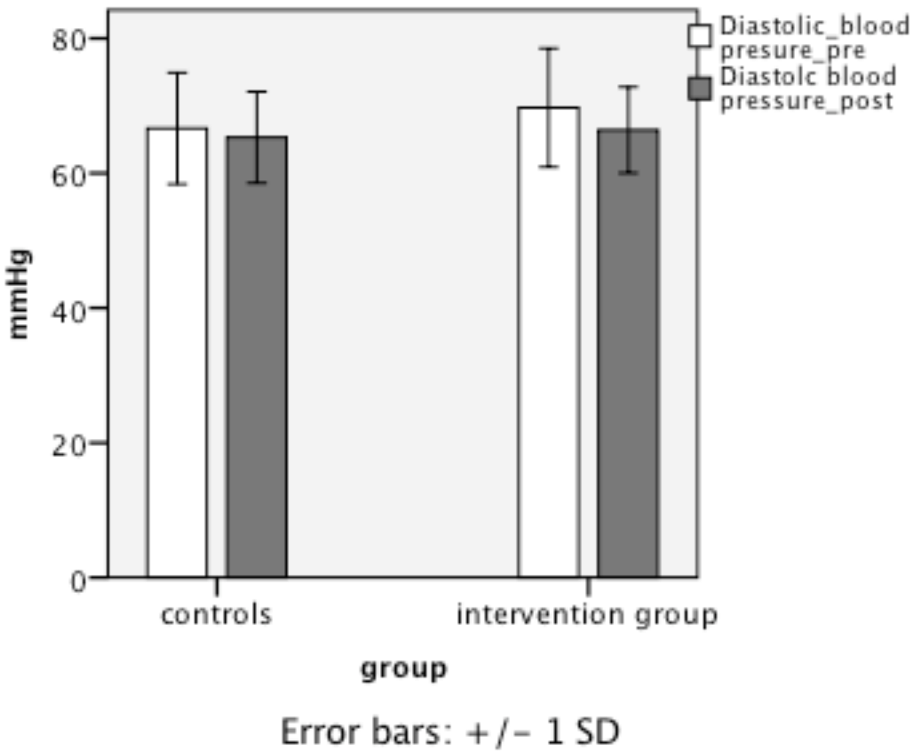

Figure 8 Development of the diastolic blood pressure from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: *P* < 0.05*; *P* < 0.01**; *P* < 0.001***).

Resting heart rate

In the intervention group the resting heart rate did not differ at baseline compared to 6 month later. At baseline the mean value was 90.17 ± 11.44 beats/minute and after the intervention 89.41 ± 12.40 beats/minute (*t* [16] = 0.472, *P* = 0.644. In the control group the resting heart rate was significantly lower in the post-test. The resting heart rate at baseline was 91.35 ± 11.43 beats/minute and by 7.61 ± 4.50 beats/minute lower at the time of the post-test (83.74 ± 15.93 beats/minute). The difference is significant (*t* [42] = 2.893, *P* = 0.006 (Figure 9).

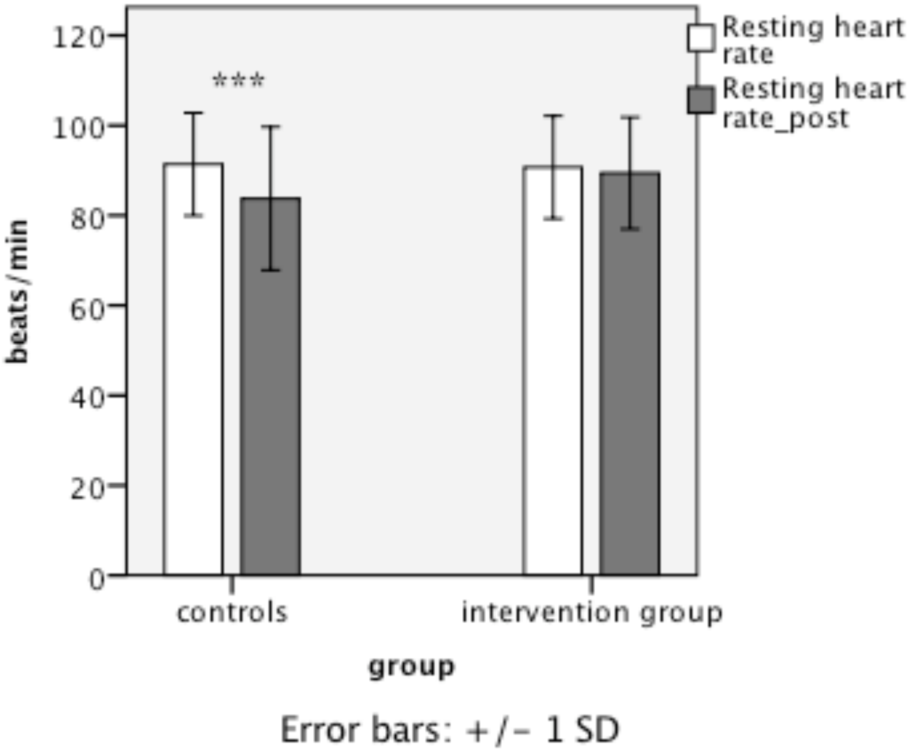

Figure 9 Development of the resting heart rate from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: *P* < 0.05*; *P* < 0.01**; *P* < 0.001***).

Intima-media thickness (IMT)

The IMT at baseline and 6 months later did not differ in the intervention group. At baseline the IMT was 0.504 ± 0.061 mm and after 6 months intervention 0.508 mm, *t* [9] = -0.159, *P* = 0.877.

However in the control group IMT significantly (*t* [25] = -2.110, *P* = 0.045) increased from 0.492 ± 0.046 mm at baseline to 0.516 ± 0.038 mm 6 months later.

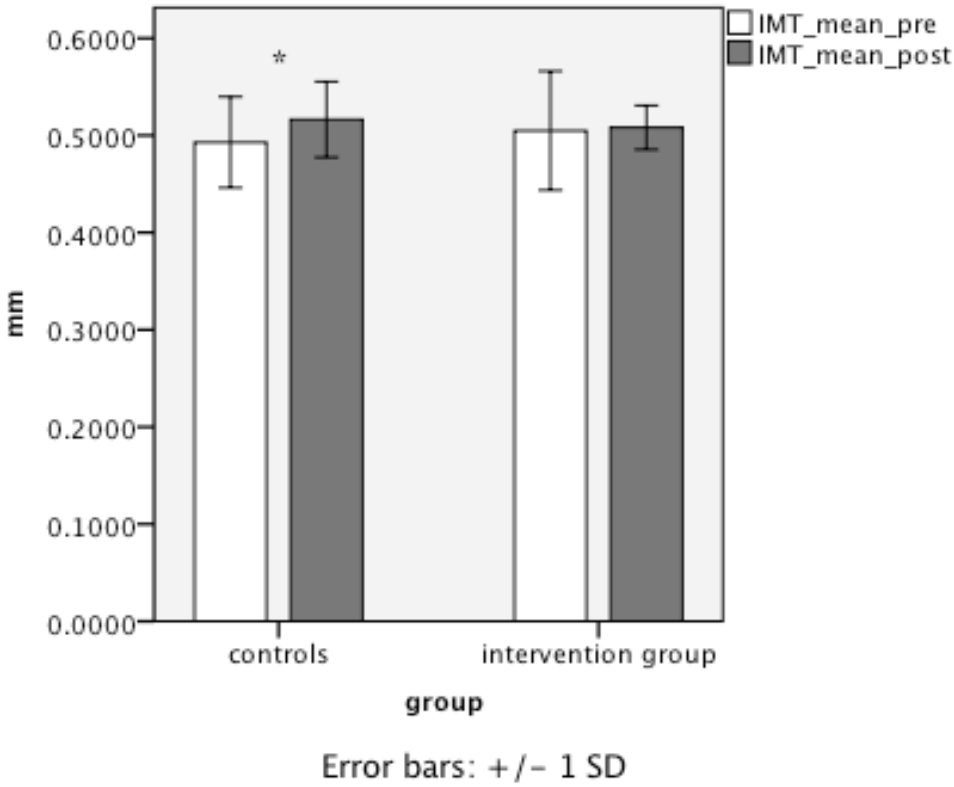

Figure 10 Development of the intima-media thickness (IMT) from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: p<0.05*; p<0.01**; p<0.001***).

Table 19 presents an overview of the anthropometrical data and cardiovascular risk factors at baseline (pre) and post of the intervention, separately for the control and intervention group.

Table 19 Summary – Overview of the anthropometric data and cardiovascular risk factors at baseline (pre) and post the intervention, separately for the control and intervention group.

Paired samples t-test. The significance level is $P \leq 0.05$.

Group		Mean	N	SD	*P* value
Controls	BMI_pre	16.35	45	2.12	0.056
	BMI_post	16.54	45	2.18	
	Body fat_pre	20.63	45	3.55	<0.001
	Body fat_post	21.47	45	3.59	
	Systolic blood pressure_pre	100.89	45	8.20	0.430
	Systolic blood pressure_post	102.00	45	6.69	
	Diastolic blood pressure_pre	66.67	45	8.25	0.215
	Diastolic blood pressure_post	65.33	45	6.77	
	Heart rate	91.35	43	11.43	0.006
	Heart rate_post	83.74	43	15.93	
	IMT_pre	0.492	26	0.046	0.045
	IMT_post	0.516	26	0.038	
Intervention group	BMI_pre	16.93	19	2.20	0.093
	BMI_post	17.27	19	2.16	
	Body fat_pre	21.12	16	3.03	0.011
	Body fat_post	22.08	16	2.95	
	Systolic blood pres-sure_pre	102.50	18	8.78	0.013
	Systolic blood pres-sure_post	106.94	18	6.21	
	Diastolic_blood pre-sure_pre	69.72	18	8.82	0.124
	Diastolc blood pres-sure_post	66.39	18	6.37	
	Heart rate	90.71	17	11.44	0.644
	Heart rate_post	89.41	17	12.40	
	IMT_pre	0.504	10	0.061	0.877
	IMT_post	0.508	10	0.022	

Effect of the intervention program on health- and skill-related physical fitness

The results of the baseline examination of physical fitness reveal no significant differences between the intervention and the control group in boys (Table 20) and also not in girls (Table 21).

Table 20 Comparison of health- and skill related physical fitness in the control and intervention group in boys at baseline.

Independent sample t-Test. The significance level is $P \leq 0.05$.

	Group	N	Mean	SD	*P* value
Sit-and-reach [cm]	Controls	23	-4.11	7.53	0.060
	Intervention group	7	1.79	4.33	
Step test [t-value]	Controls	23	38.30	9.27	0.109
	Intervention group	7	45.29	11.45	
Bent-arm hang [sec]	Controls	23	16.15	12.17	0.599
	Intervention group	7	13.57	6.70	
Sit-ups [n]	Controls	23	20.78	5.42	0.532
	Intervention group	7	22.14	2.73	
Tapping [Hz]	Controls	23	8.78	1.23	0.583
	Intervention group	7	9.06	.77	
Drop jumps [msec]	Controls	22	167.95	42.55	0.887
	Intervention group	7	165.42	32.85	
Acceleration [0-10) [sec]	Controls	23	2.15	.13	0.732
	Intervention group	7	2.13	.10	
Coordination run [sec]	Controls	23	7.61	1.10	0.666
	Intervention group	7	7.41	.85	
Speed (10-20m) [sec]	Controls	23	1.79	.15	0.932
	Intervention group	7	1.78	.10	

Continuation of Table 20

	Group	N	Mean	SD	*P* value
Simple reaction test [msec]	Controls	22	515.54	94.97	0.669
	Intervention group	7	533.28	92.75	
Complex reaction test [sec]	Controls	23	30.46	8.11	0.698
	Intervention group	7	29.21	3.75	

Table 21 Comparison of health- and skill related physical fitness in the control and intervention group in girls at baseline.

Independent sample t-Test. The significance level is $P \leq 0.05$.

	Group	N	Mean	SD	*P* value
Sit-and-reach [cm]	Controls	22	1.92	5.95	0.789
	Intervention group	11	1.32	6.31	
Step test [t-value]	Controls	22	39.66	10.20	0.110
	Intervention group	12	34.63	3.63	
Bent-arm hang [sec]	Controls	22	11.33	7.68	0.442
	Intervention group	12	9.24	7.02	
Sit-ups [n]	Controls	22	19.09	4.55	0.411
	Intervention group	12	20.42	4.18	
Tapping [Hz]	Controls	22	7.50	1.65	0.059
	Intervention group	12	8.58	1.25	
Drop jumps [msec]	Controls	22	173.36	35.94	0.549
	Intervention group	12	181.66	42.13	
Acceleration (0-10m) [sec]	Controls	22	2.18	.13	0.947
	Intervention group	12	2.19	.12	

Continuation of Table 21

	Group	N	Mean	SD	*P* value
Coordination run [sec]	Controls	22	7.91	.69	0.437
	Intervention group	12	7.67	1.02	
Speed (10-20m) [sec]	Controls	22	1.82	.14	0.545
	Intervention group	12	1.79	.10	
Simple reaction test [msec]	Controls	21	566.80	123.57	0.685
	Intervention group	12	550.41	82.19	
Complex reaction test [sec]	Controls	22	30.74	5.20	0.974
	Intervention group	12	30.79	3.97	.

Table 22 Levene's test for equality of error variances between the control and intervention group.

The significance level is $P \leq 0.05$.

Variable	*F* [df 1, 2]	*P* value
Sit-and-reach [cm]	1.177 [df 3, 59]	0.326
Step test [t-value]	2.954 [df 3, 60]	0.040*
Bent-arm hang [sec]	3.056 [df 3, 60]	0.035*
Sit-ups [n]	0.793 [df 3, 60]	0.503
Tapping [Hz]	1.446 [df 3, 60]	0.239
Drop jumps [msec]	0.596 [df 3, 59]	0.620
Acceleration (0-10 m) [sec]	0.789 [df 3, 60]	0.505
Coordination run [sec]	1.062 [df 3, 60]	0.372
Speed (10-20 m) [sec]	0.760 [df 3, 60]	0.521
Simple reaction test [msec]	0.187 [df 3, 58]	0.905
Complex reaction test [sec]	0.524 [df 3, 60]	0.667

The Leven's test revealed that the homogeneity of variance of the dependent variables "step test [t-value]" and bent-arm hang [sec] are significant, which means that there is significant interaction between the factors. The assumption of homogeneity of variance was violated, therefore the Welch *F* – ratio is reported for these two variables.

Table 23 Results of the univariate analysis of variance to test effects of sex and group affiliation on health- and skill-related fitness parameters at baseline

Dependent variable	**Fixed factors**	***F*** **[df 1, 2]**	***P* value**
Sit-and-reach [cm]	Sex (male; female)	2.261 [df 3, 59]	0.138
	Group (intervention; control group)	2.043 [df 3, 60]	0.158
Step test [t-value]	Sex (male; female)	0.747 [df 1, 57.93]	0.391
	Group (intervention; control group)	0.027 [df 1, 36.50]	0.870
Bent-arm hang [sec]	Sex (male; female)	4.298 df [1, 49.63]	0.043*
	Group (intervention; control group)	1.740 df [1, 49.27	0.193
Sit-ups [n]	Sex (male; female)	1.683 [df 3, 60]	0.199
	Group (intervention; control group)	1.039 [df 3, 60]	0.312
Tapping [Hz]	Sex (male; female)	5.307 [df 3, 60]	0.025
	Group (intervention; control group)	3.100 [df 3, 60]	0.083
Drop jumps [msec]	Sex (male; female)	0.956 [df 3, 60]	0.332
	Group (intervention; control group)	0.068 [df 3, 60]	0.795
Acceleration (0-10 m [sec]	Sex (male; female)	1.255 [df 3, 59]	0.267
	Group (intervention; control group)	0.050 [df 3, 60]	0.823

Continuation of Table 23

Dependent variable	**Fixed factors**	***F* [df 1, 2]**	***P* value**
Coordination run [sec]	Sex (male; female)	1.156 [df 3, 60]	0.287
	Group (intervention; control group)	0.671 [df 3, 60]	0.416
Speed [sec]	Sex (male; female)	0.378 [df 3, 60]	0.541
	Group (intervention; control group)	0.191 [df 3, 60]	0.664
Simple reaction test [msec]	Sex (male; female)	1.369 [df 3, 60]	0.247
	Group (intervention; control group)	0.001 [df 3, 60]	0.942
Complex reaction test [sec]	Sex (male; female)	0.289 [df 3, 60]	0.593
	Group (intervention; control group)	0.119 [df 3, 60]	0.731

A significant effect of sex on the bent-arm hang sustained, F [1, 49.63] = 4.298, *P* = 0.043. On all other tested variables the fixed factors sex and group affiliation revealed no significant effect.

Health- and skill related-fitness at baseline and 6 months later

Children in the control and intervention group significantly increased their performances in almost all physical fitness tests. Only in hamstring, gluteal and lower back muscle flexibility (sit-and-reach), in upper body muscular endurance strength (bent-arm hang), and in reactive strength (drop jumps) the test results did not change significantly after the intervention program, neither in the intervention, nor in the control group.

Sit-and-reach test – assessment of hamstring, gluteal and lower back muscle flexibility

Figure 11 shows the test results of the sit-and-reach test of the control and intervention group at the baseline (pre-test) and 6 months later, post the intervention.

There was no significant difference in harmstring, gluteal and lower back muscle flexibility at baseline and 6 months later. In the intervention group the sit-and reach performance slightly increased from 1.50 ± 5.48 cm to 1.84 ± 6.82 cm, however the increase was not significant, t [18] = -8.13, P = 0.427.

In the control group the flexibility also slightly increased from -1.16 ± 7.38 cm to 0.68 ± 8.23 cm, however, the increase was not significant, t [44] = - 2.008, *P* = 0.051 (Figure 11).

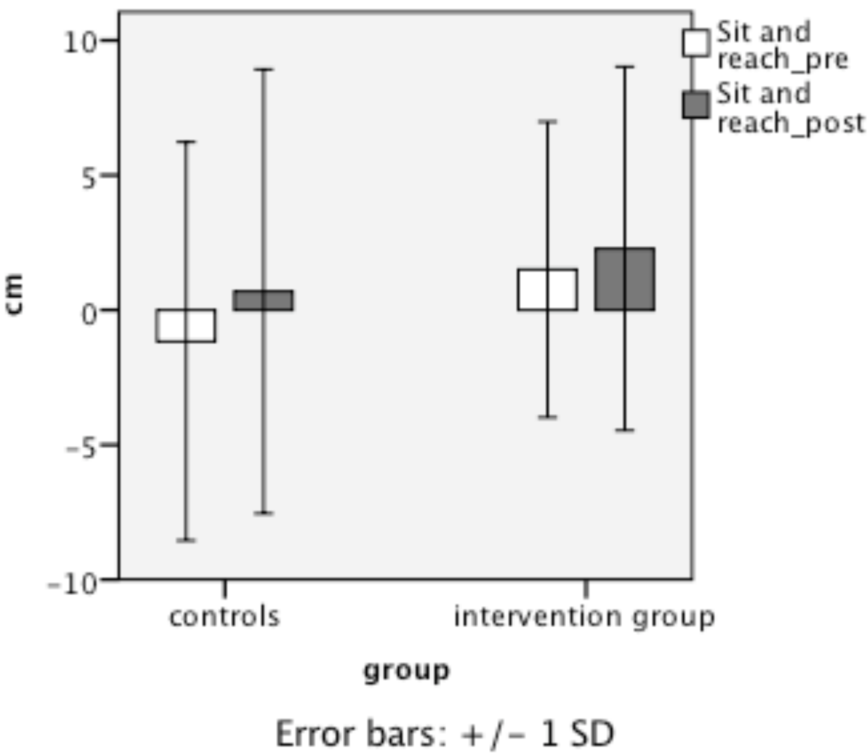

Figure 11 Development of hamstring, gluteal and lower back muscle flexibility test (sit-and-reach) from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: p<0.05*; p<0.01**; p<0.001***).

Step test - assessment of anaerobic cardiorespiratory endurance

The children of the intervention and of the control group both significantly increased ($p<0.01$) their performance. The intervention group increased their performance (t-value) from 38.55 ± 8.93 to 53.86 ± 8.55, t [18] = -6.022, P < 0.0011. However the control group also increased their respiratory performance from 38.94 ± 9.75 to 58.42 ± 4.74 (t-value) t [43] = -11.792, P <0.001.

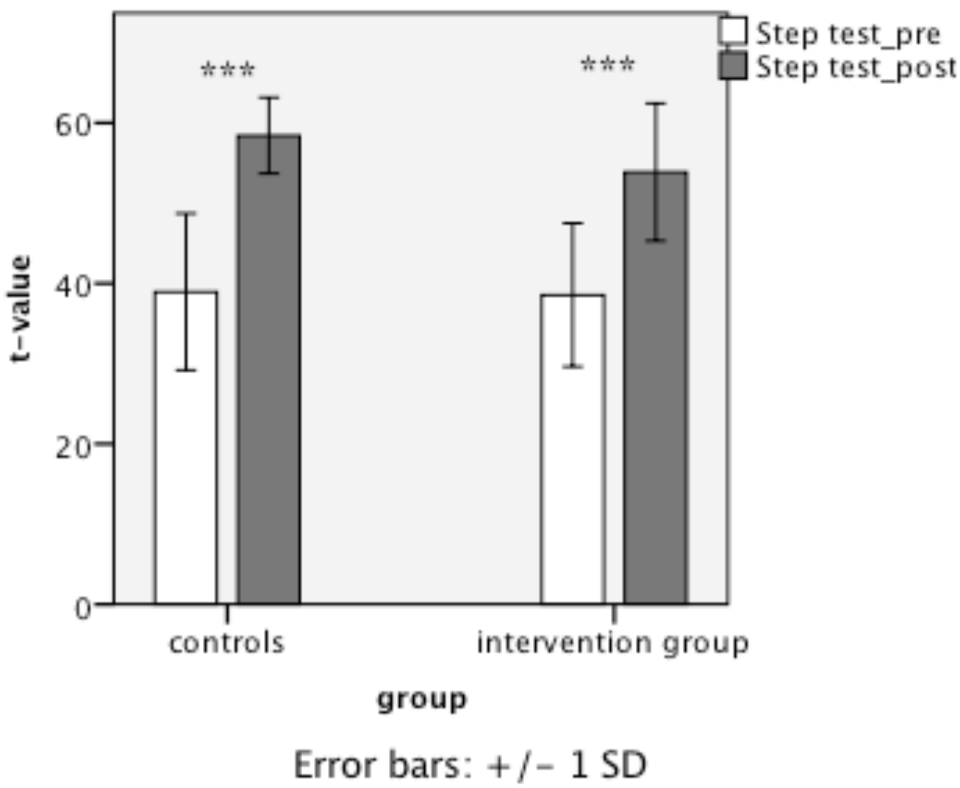

Figure 12 Development of cardiorespiratory endurance (step test) from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: P < 0.05*; P < 0.01**; P < 0.001***).

Bent-arm hang – assessment of upper trunk muscular endurance strength

The intervention group performed a hang time of 10.84 ± 7.05 sec at baseline and in the post-test 10.05 ± 5.53 sec. This reduction is not significant t [18] = 0.750, P = 0.463

The control group performed a mean hang time of 14.03 ± 10.41 in the pre-test.

With a hang time of 15.20 ± 12.41 sec in the post test, there is no difference between pre and post examination, t [43] = -1.568, P = 0.249) (Figure 13).

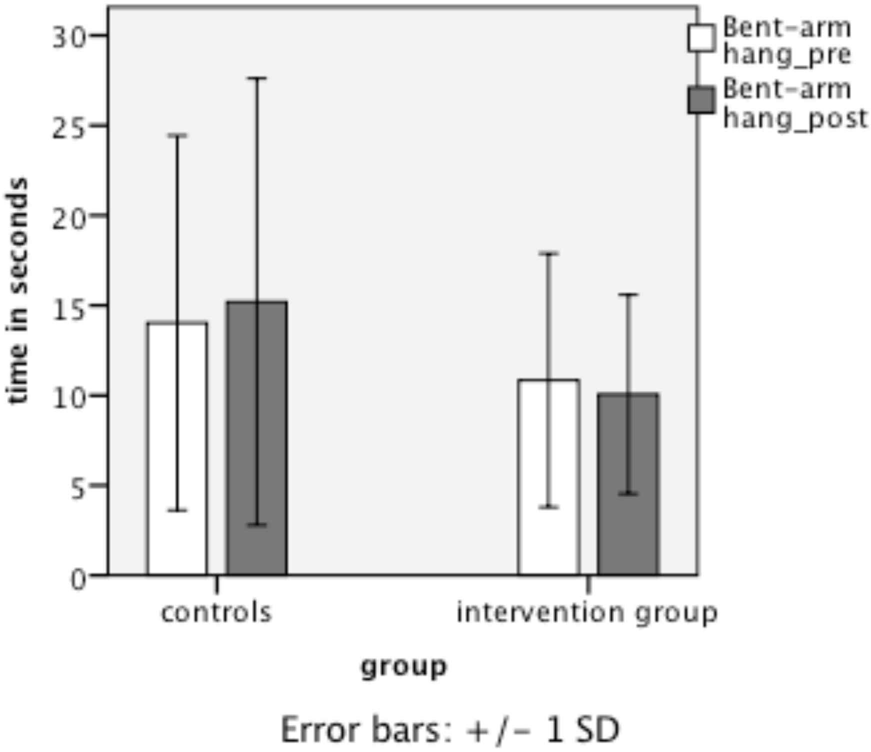

Figure 13 Development of upper trunk muscular endurance strength (bent-arm hang) from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: $P < 0.05$*; $P < 0.01$**; $P < 0.001$***).

Sit-ups – assessment of abdominal muscular endurance strength

The children of the intervention and of the control group both significantly increased their test performance comparing the baseline and the post-test 6 months later. The intervention group performed a number of 21.05 ± 3.73 sit-ups at baseline and increased significantly (t [18] = -5.704, *P* <0.001) up to a number of 24.63 ± 4.03 sit-ups.

The control group significantly (t [44] = -4.211, *P* < 0,001) increased from a number of 19.96 ± 5.03 to a number of 23.15 ± 4.70 sit-ups (Figure 14).

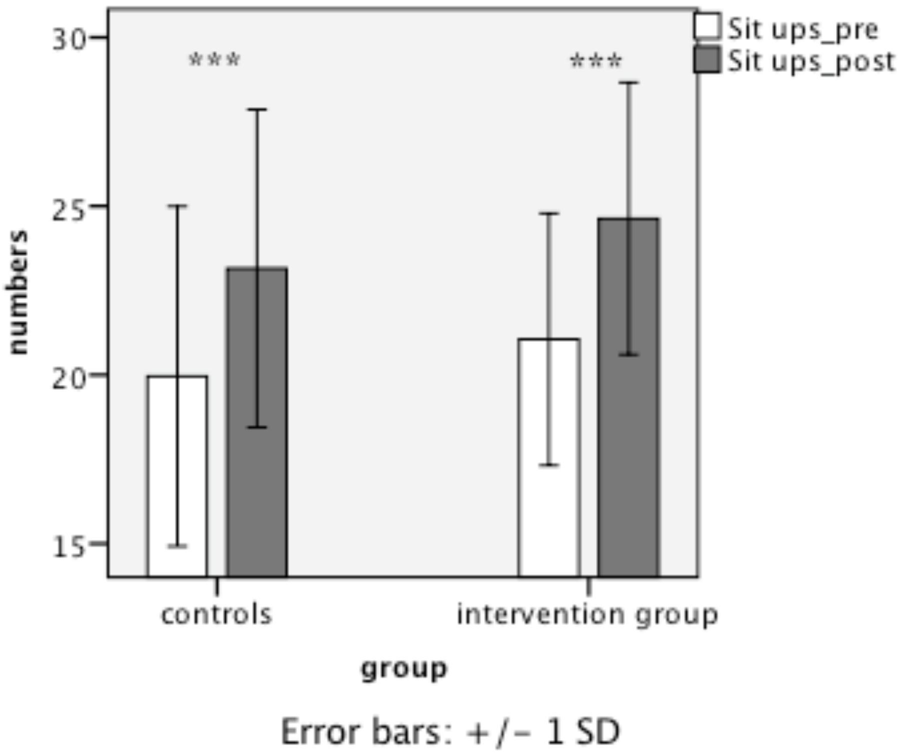

Figure 14 Development of abdominal muscular endurance strength (sit-ups) from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: *P* < 0.05*; *P* < 0.01**; *P* < 0.001***).

Tapping – assessment of speed of limb movement

In the tapping test, the children of the intervention and of the control group significantly increased their performance comparing the results at baseline and post examination. The intervention group significantly (t [17] = -5.347, $P < 0.001$) increased from 8.75 ± 1.13 Hz to 10.16 ± 1.39 Hz. Whereas, the children of the control group also increased their performance from 8.15 ± 1.57 Hz to 9.22 ± 1.05 Hz. t [44] = -7.885, $P < 0.001$ (Figure 15).

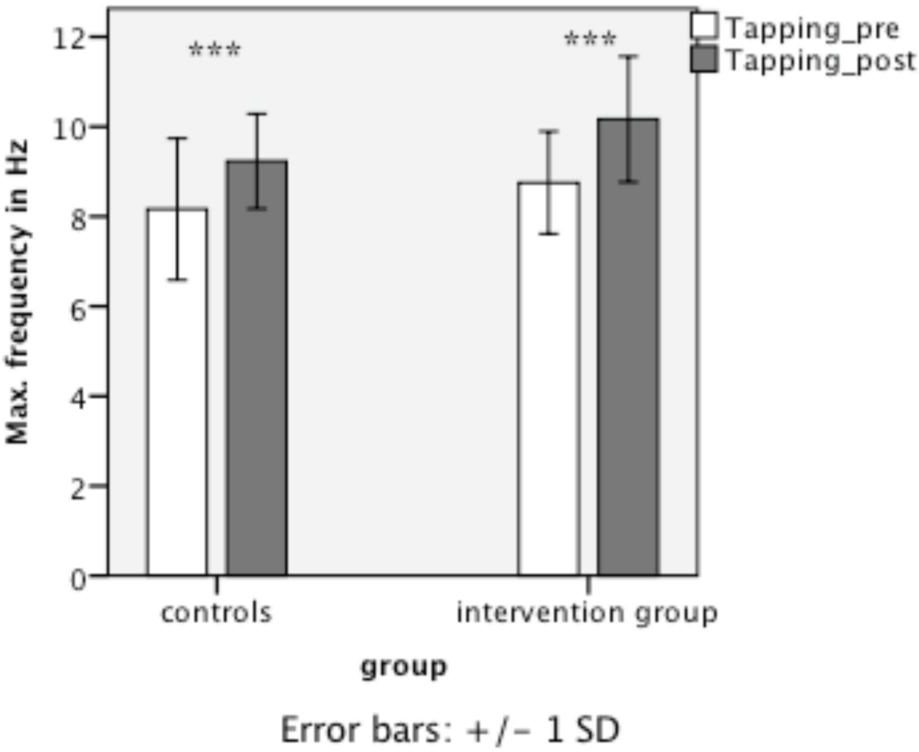

Figure 15 Development of speed of limb movement (tapping) from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: $P < 0.05$*; $P < 0.01$**; $P < 0.001$***).

Drop jumps – assessment of reactive strength

Comparing the results of the pre and post-test of the intervention and control group, no significant differences could be described (pre-test: p=0.640; post-test p=0.560) in the ground contact time during drop jumping. The intervention group minimally increased the ground contact time from 169.81 ± 36.03 msec to 174.44 ± 70.35 msec, t [15] = -0.269, *P* = 0.792 and the control group also minimally increased the contact time from 171.92 ± 39.54 msec to 184.63 ± 52.88 msec, t [40] = -1.305, *P* = 0.199) (Figure 16).

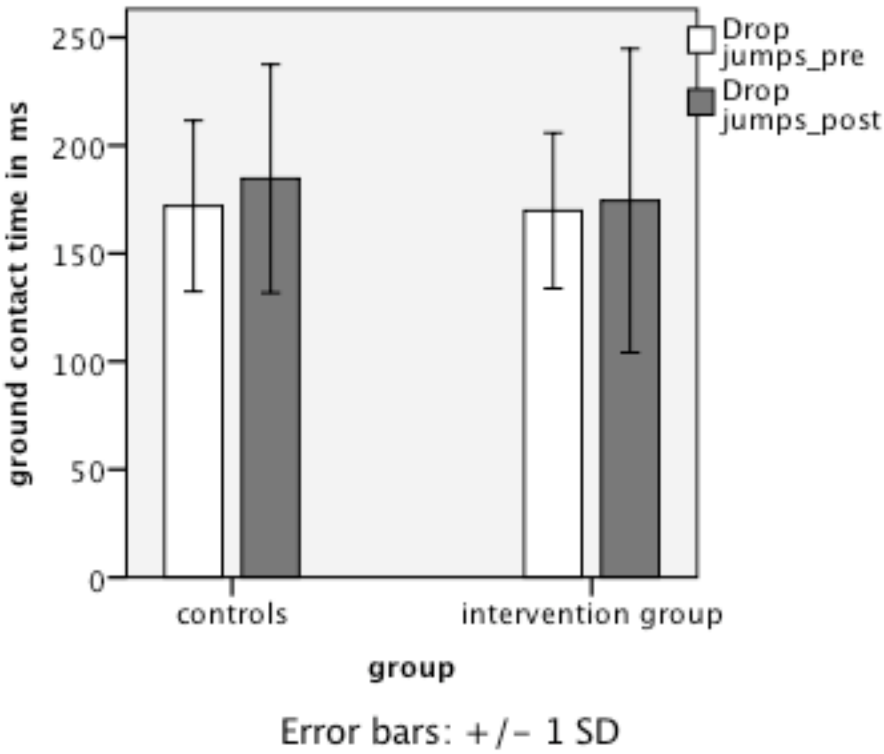

Figure 16 Development of reactive strength (drop jumps) from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: *P* < 0.05*; *P* < 0.01**; *P* < 0.001***).

20 meters run – assessment of speed and 0 - 10 m acceleration

The results of the 20m running test are separated into 0-10 meters acceleration performance and 10 – 20 m speed performance. Results are presented in Figure 17 and 18.

The children of the intervention group significantly (t [18] = 3.209, P = 0.005) increased their acceleration from 2.17 ± 0.12 sec to 2.09 ± 0.12 sec.

Also the control group significantly increased their acceleration performance from 2.17 ± 0.13 sec to 2.09 ± 0.12 sec, t [44] = 5.371, P <0.001 (Figure 17).

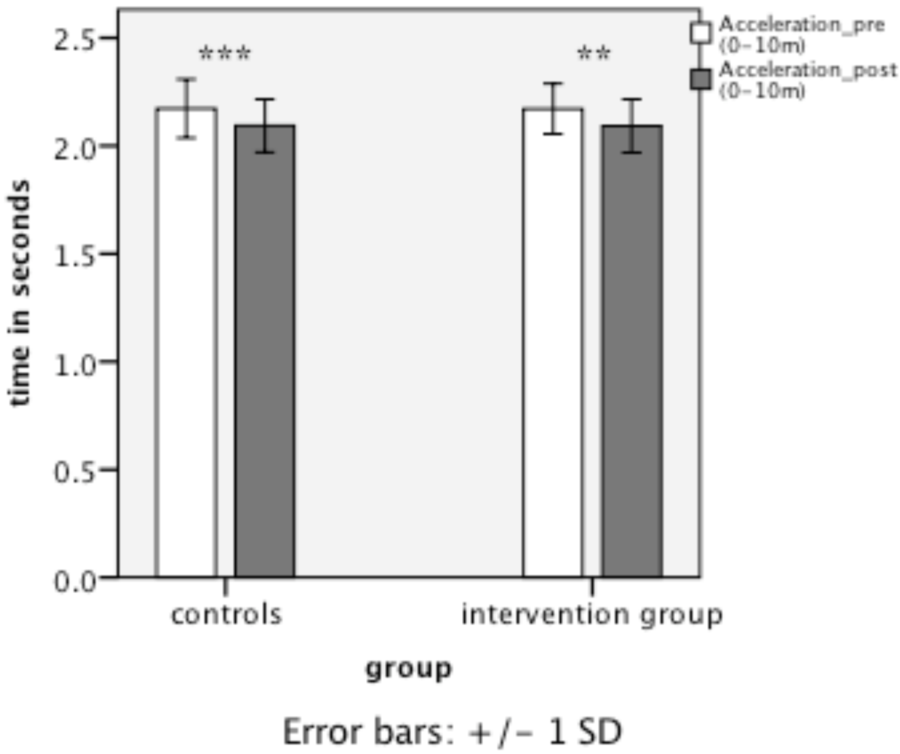

Figure 17 Development of acceleration (0-10 m) from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: *P* < 0.05*; *P* < 0.01**; *P* < 0.001***).

After the basketball intervention children run significantly faster on the 10 – 20 meters from 1.79 ± 0.10 sec to 1.75 ± 0.10 sec, t [18] = 2.490, $P = 0.023$).

The control group also ran significantly faster from 1.80 ± 0.14 sec. to 1.74 ± 0.11 sec (t [44] = 4.567, $P < 0.001$) (Figure 18).

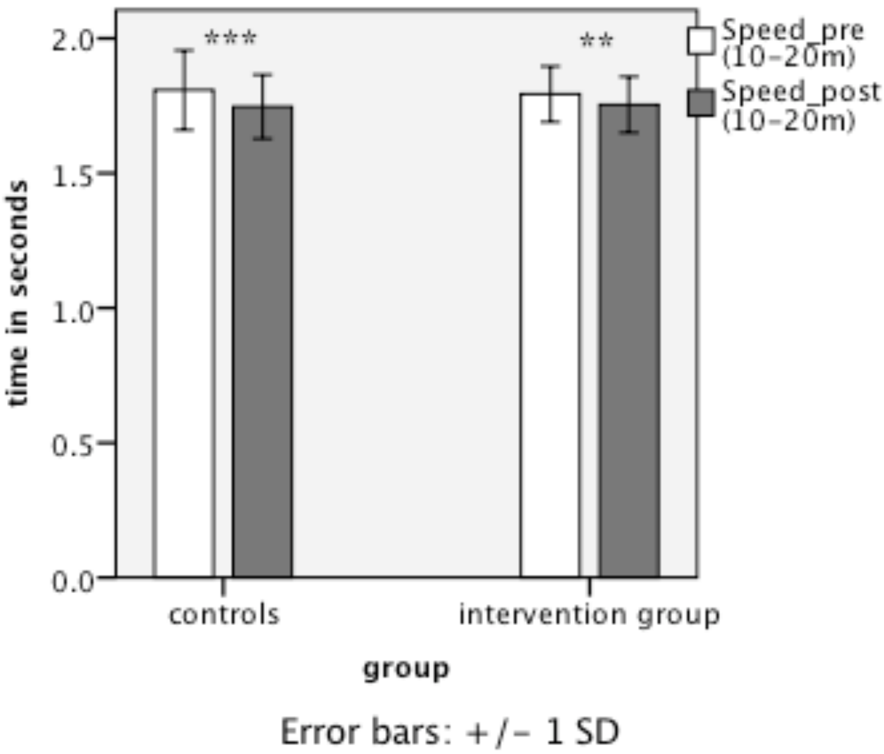

Figure 18 Development of speed (10-20 m) from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: $P < 0.05$*; $P < 0.01$**; $P < 0.001$***).

10 m coordination run – assessment of running coordination and speed

Looking at the effect of the intervention the children of the intervention group ran faster, significantly reducing their running time from 7.58 ± 0.95 sec in the entrance examination down to 6.99 ± 0.70 sec. (t [18] = 4.015, *P* = 0.003) in the post test.

The control group also significantly reduced their running time from a mean time of 7.75 ± 0.92 in the pre-test down to 7.26 ± 0.83 (p<0.001) in the post-test, t [44] = -4.453, P <0.001 (Figure 19).

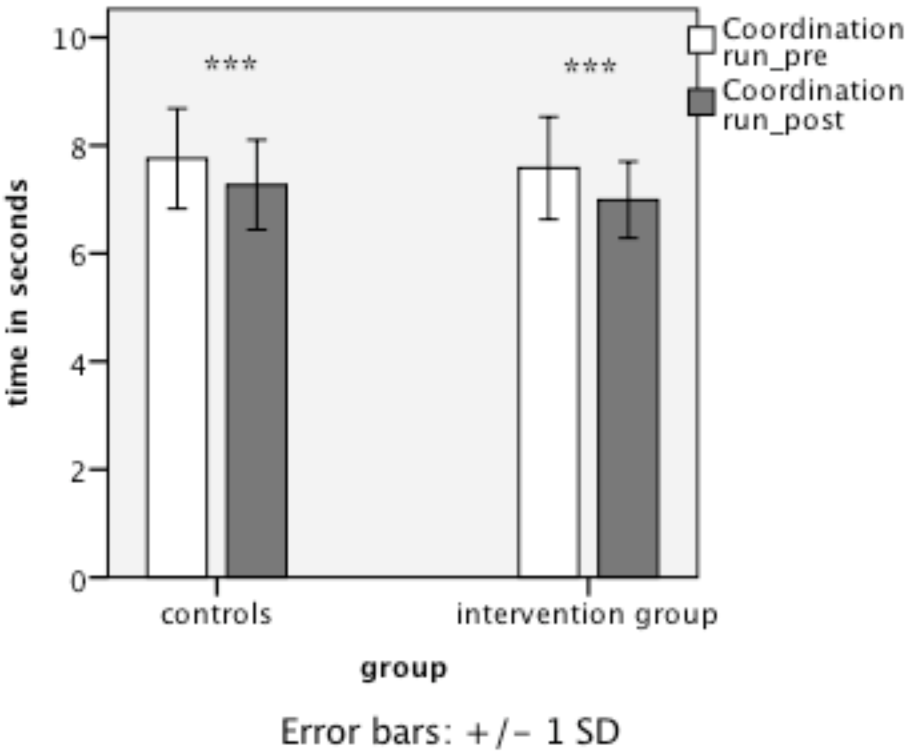

Figure 19 Development of running coordination and speed (coordination run) from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: *P* < 0.05*; *P* < 0.01**; *P* < 0.001***).

Simple reaction test – assessment of coordination and visual reaction time

In the simple reaction test of coordination and reaction time both groups significantly increased their test performances. In detail the children of the intervention group reacted faster from a mean reaction time of 544.10 ± 84.07 msec down to 494.58 ± 71.60 msec (t [18] = 3.360, *P* = 0.003).

The test results of the control group showed the same tendency. The mean reaction time was 540.58 ± 111.59 msec at baseline and 508.93 ± 76.51 msec in the post-test (t [42] = 2.085, *P* = 0.043) (Figure 20).

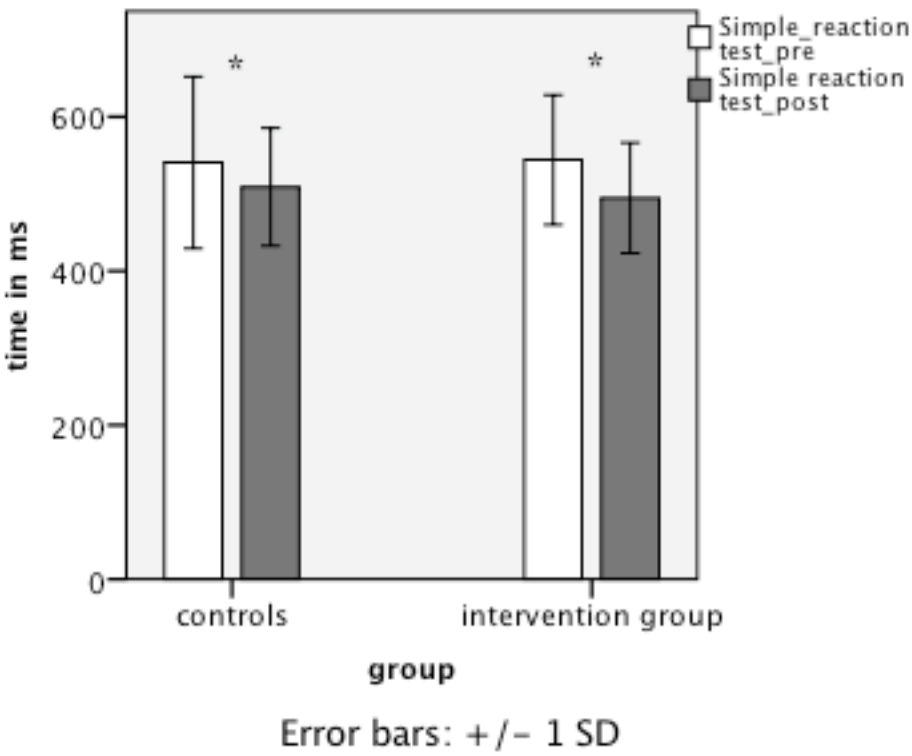

Figure 20 Development of simple reaction from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: $P < 0.05$*; $P < 0.01$**; $P < 0.001$***).

Complex reaction test – assessment of coordination and reaction time

After the intervention, the children of the intervention group significantly (t [18] = 14.551, *P* < 0.001) performed significantly better by reducing their coordination and reaction time from a mean time of 30.21 ± 3.86 sec down to a faster mean time of 22.16 ± 2.49 sec.

Very similarly the control group performed significantly (t [44] = 13.620, *P* < 0.001) better and reduced their reaction time from a mean of 30.60 ± 6.77 sec to a faster mean time of 23.00 ± 4.53 sec (Figure 21).

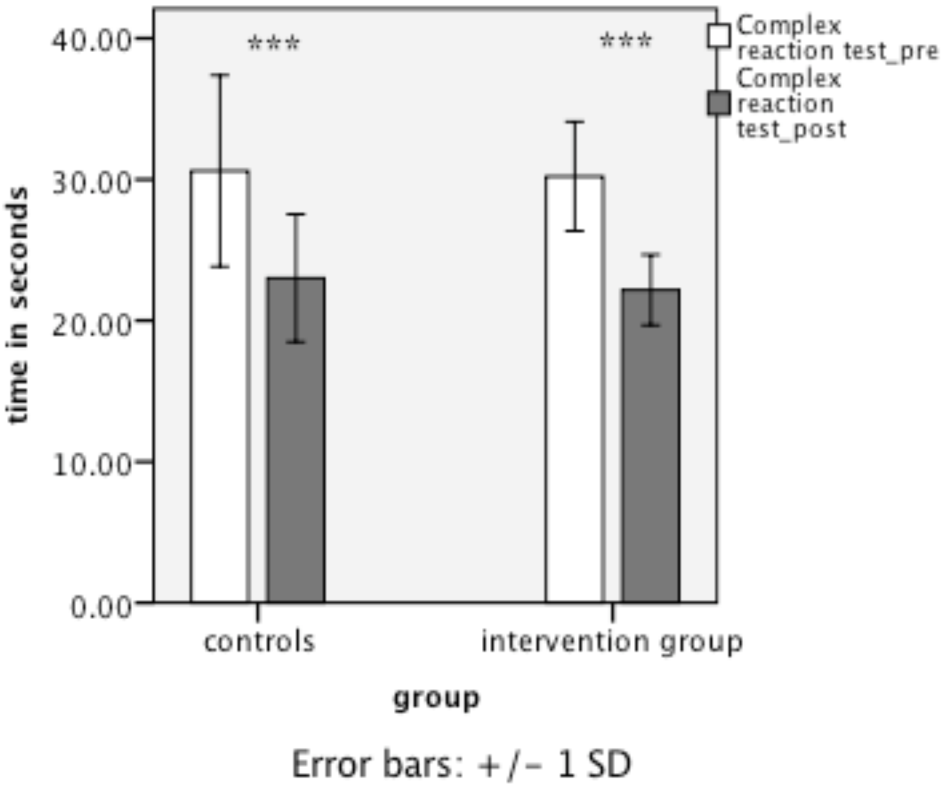

Figure 21 Development of coordination and reaction time (complex reaction test) from pre (baseline) to post examination, separately displayed for the intervention and control group.

(Significant differences: *P* < 0.05*; *P* < 0.01**; *P* < 0.001***).

The following Table 24 is summarizing the results of the health- and skill-related physical fitness test at baseline (pre) and post intervention. Results are presented for the control and intervention group.

Table 24 Summary – Overview of the sport motor fitness test at baseline (pre) and post the intervention, separately for the control and intervention group

Group		Mean	N	SD	*P* value
Controls	Sit-and-reach_pre [cm]	-1.16	45	7.38	0.051
	Sit-and-reach_post [cm]	.68	45	8.23	
	Step test _pre [t-value]	38.94	45	9.75	<0.001
	Step test_post [t-value]	58.42	45	4.74	.
	Bent-arm hang_pre [sec]	14.03	45	10.41	0.249
	Bent-arm hang_post [sec]	15.20	45	12.41	
	Sit-ups_pre [n]	19.96	45	5.03	<0.001
	Sit-ups_post [n]	23.15	45	4.70	
	Tapping_pre [Hz]	8.16	45	1.57	<0.001
	Tapping_post [Hz]	9.22	45	1.05	
	Drop jumps_pre [ms]	171.92	45	39.54	0.199
	Drop jumps_post [ms]	184.63	45	52.88	
	Acceleration_pre (0-10m) [sec]	2.17	45	.13	<0.001
	Acceleration_post (0-10m) [sec]	2.09	45	.12	
	Speed_pre (10-20m) [sec]	1.80	45	.14	<0.001
	Speed_post (10-20m) [sec]	1.74	45	.11	
	Coordination run_pre [sec]	7.75	45	.92	<0.001
	Coordination run_post [sec]	7.26	45	.83	

Continuation of Table 24

Group		Mean	N	SD	*P* value
	Simple_reaction test_pre [ms]	540.58	45	111.59	0.043
	Simple reaction test_post [ms]	508.93	45	76.51	
	Complex reaction test_pre [sec]	30.60	45	6.77	<0.001
	Complex reaction test_post [sec]	23.00	45	4.53	
Intervention group	Sit-and-reach_pre [cm]	1.50	19	5.48	0.427
	Sit-and-reach_post [cm]	1.84	19	6.82	
	Step test _pre [t-value]	38.55	19	8.92	<0.001
	Step test_post [t-value]	53.86	19	8.55	
	Bent-arm hang_pre [sec]	10.84	19	7.05	0.463
	Bent-arm hang_post [sec]	10.05	19	5.53	
	Sit-ups_pre [n]	21.05	19	3.73	<0.001
	Sit-ups_post [n]	24.63	19	4.03	
	Tapping_pre [Hz]	8.75	19	1.13	<0.001
	Tapping_post [Hz]	10.16	19	1.39	
	Drop jumps_pre [ms]	169.81	19	36.03	0.792
	Drop jumps_post [ms]	174.44	19	70.35	
	Acceleration_pre (0-10m) [sec]	2.17	19	.11	0.005
	Acceleration_post (0-10m) [sec]	2.09	19	.12	
	Speed_pre (10-20m) [sec]	1.79	19	.10	0.023
	Speed_post (10-20m) [sec]	1.75	19	.10	
	Coordination run_pre [sec]	7.58	19	.95	0.001
	Coordination run_post [sec]	6.99	19	.70	

Continuation Table 24

Group		Mean	N	SD	*P* value
	Simple_reaction test_pre [ms]	544.10	19	84.07	0.003
	Simple reaction test_post [ms]	494.58	19	71.60	
	Complex reaction test_pre [sec]	30.21	19	3.86	<0.001
	Complex reaction test_post [sec]	22.16	19	2.49	

6.1.4 Discussion

Physical inactivity has been identified as an independent risk factor for coronary heart disease[228]. Adequate interventions in primary schools may help to increase physical activity and fitness at an early stage[229]. Since obesity and physical inactivity are increasingly seen as a problem in childhood, schools could play a key role in encouraging a healthy lifestyle[230].

Major reviews by Blair[45] and Pate[231] identified physical inactivity as a serious problem and major public concern for youth and adults. Furthermore, physical inactivity leads to less physical fitness[74]. Since physical activity and health behavior track into adulthood[173,232,233] it is important to promote physical activity and thereby improve physical fitness in young children. Further it has been stated by the WHO that collaboration among school, home and community (e.g. sports clubs) is important since different political aims could be cleared by a shared language and a shared way of working and understanding each other[234].

An example for such a network is the present “Sport passed 1 o’clock program” initiated by the Bavarian Ministry of Environment and Public Health, with the main aim to promote physical activity.

The SV Germering launched a basketball training program in cooperation with the primary schools in Germering. The main aim of this initiative was to get children involved in a sport and affiliated to a sport club, with the idea of increasing physical activity and physical fitness, social interaction and through this affiliation supporting long-term cardiovascular prevention.

The study aim was to investigate whether a participation in the "Sport past 1 o'clock program" improves cardiovascular risk factors and results is an increase of health-related and skill-related physical fitness.

Interventional effects on anthropometrical and cardiovascular parameters

The results of the study revealed that there were no differences in anthropometric parameters and cardiovascular risk factors between the intervention and the control group at baseline.

After the intervention the children slightly increased their BMI and significantly increased their total percentage of body fat. These results are similar in the control group. The children slightly increased their BMI and significantly increased their total percentage of body fat. Additionally the percentage of increase did not differ significantly between the groups. Therefore, it can be stated that this results are due to a normal maturation of the children within the study period of 6 months.

The present results are in line with the reports of the German CHILT project[235]. After much longer intervention of 4-years a difference in the prevalence of overweight and obese children between the experimental schools and control schools could not be proven. The authors concluded that preventive interventions in primary schools offers an effective means to improve selected coordinative skills, but does not influence the incidence of overweight and obesity, when parents were not included in the intervention[235]. Contradictory findings were reported by a Greek study of Manios and colleagues[236,237] who reported a significant reduced increase of BMI and improvement of fitness after a much longer intervention period of 3 or 6 years of school interventions in Cretan primary school children, who were 6 years of age at baseline. Furthermore the "Dance for Health"[238] intervention revealed positive results in girls only. 150 minutes of dance per week resulted in a decrease of BMI in girls. Another Australian cardiovascular risk prevention study[239] described a successful intervention in the group of children that were in the intervention group receiving the modules school nutrition and physical fitness. They authors described a significant change in triceps-skin fold change after a duration of 12 months.

In general, it has been stated that physical activity is shown to be effective as prevention against cancer, type II diabetes and cardiovascular disease, even when weight was not reduced[240].

Blood pressure and heart rate

In the present study, systolic blood pressure was significantly increased, diastolic blood pressure revealed no significant difference after the intervention.

There was also no difference in the mean resting heart rate between baseline and post interventional examination.

In the control group, no difference in systolic and diastolic blood pressure as well as heart rate was examined after 6 months.

Results of the large CATCH study, involving 5000 children with an entry age of 8.8 years, were unable to demonstrate a change in blood pressure, although students reported a significant enhancement of physical activity[153]. The intervention was mainly dietary and enhancement of physical education at school.

In young children, the effects of physical activity on cardiovascular risk factors are less clear and overall the results are not strong, with cross-sectional data reporting both, some effects and no effect of childhood physical activity[241]. Studies of Despres and colleagues[242] demonstrated poorer fitness with unfavorable blood pressure.

In the Heart Smart Project, as a part of the Bogalusa Heart Study, the authors even suggested that cardiovascular risk factors remain better correlates with fatness, rather than fitness[243].

IMT

Regarding the effects of the basketball training on the vascular system, no significantly change of IMT after the intervention program was examined.

Differently in the control group, the IMT significantly increased from baseline to the post examination 6 months later.

This result is remarkable since all other anthropometric and traditional cardiovascular risk factors did not differ between intervention and control group. However, the study population is small so that it could only carefully be suggested that this is an effect of the additional training within the basketball intervention.

Ishuzi and co-workers[244] described a correlation of IMT and age in 8 – 10 year – old children, whereas the IMT increased by 0.04mm in boys and 0.02 mm in girls within the 2 years.

Interventional effects on health- and skill-related physical fitness

Both groups significantly increased their performances all assessed physical fitness components. Therefore it could not be stated that the improvement in health- and skill related physical fitness results from the basketball program. Reynolds et al 1990 described the benefits from training for skill development, whereas the acquisition of essential skills promoted self-efficacy, which is a major predictor of physical activity. As previously reported, Graf and colleagues[235] emphasized the increase of selective coordinative skills due to a physical activity intervention program.

The Franingham Childrens' Study also revealed an improvement in motor abilities for the entire studied population examined. In the study the intervention schools appeared to perform better than the control schools. However, this effect was restricted to normal weight and underweight children[245].

Positive effects on motor abilities could also be stated by an Australian study. In the "Move it groove it" intervention program physical education lessons in schools were optimized, resulting in improved motor abilities of the primary school children[246].

However, from the results of the present pilot study it is obvious that one bound of additional exercise within the school-schedule is not enough to clearly improve cardiovascular risk factors. Recommendations of the American Heart Association and others[247,248] stated that the time of physical activity for children should be at least 60 minutes per day. Graf and co-workers[249] reported German recommendations by developing a physical activity pyramid for children. The main idea of the physical activity pyramid was, to target daily activities and intensive leisure activities of 2 hours per day. Additionally, media use should be reduced to on hour per day for children younger than 12 years old.

In the relatively young and healthy population of the Amsterdam Growth and Heart Study during adolescents physical inactivity was the most important lifestyle parameter related to high risk of cardiovascular disease[88].

6.1.5 Limitations of the study

Since it was a requested evaluation of an existing program, 12 children had already participated in the basketball-training group and therefore stayed in the intervention group. 8 children were randomly selected from the participants at baseline. However, the statistical group comparison at baseline revealed no significant differences in all measured parameters between intervention and control group.

Due to financial reasons, there was no intervention or education program, involving parents and families. Further no dietary intervention was involved on the program.

The basketball intervention was not controlled for the training intensity. Future physical activity and exercise-orientated interventions should guarantee a certain training load, possibly controlled by the measurement of heart rates during the training.

Unfortunately, within the present pilot study, long-term effects could not be examined. During the evaluation the basketball coach was financed by the Ministry of Environment and Public Health. After the evaluation of the program, no sponsorship was found to continue the positive network between the sport club and the schools. This resulted in the fact that the “Sport past 1 o’clock program” had to be stopped after 12 months due to financial reasons.

6.1.6 Conclusions

It has been previously stated that adequate interventions in primary schools may help to increase physical activity and physical fitness in children at an early stage[229]. The “Sport past 1 o’clock program” of the Bavarian Ministry of Environment and Public Health demonstrated a successful network between community policies and programs with sports clubs and schools. The results could reveal a significant improvement of vascular structure but could not further reveal significant effects on traditional cardiovascular risk factors. The program further improved mainly basketball-related and trained skills such as tapping, reactive strength, flexibility and abdominal strengths. However, the children of the control group also increased their performance. The increase health- and skill-related physical fitness could be an effect of normal maturation over 6 months. It further underlines that one bound of additional exercise in not enough for a significant improvement in fitness in relation to the control group.

7 Future considerations

7.1 Non-invasive cardiovascular risk screening in pediatrics– linking arterial structure and function with physical fitness, exercise and physical actvity

Traditional cardiovascular risk factors act early in life and have a major impact on the development of atherosclerosis[17]. The results of the PDAY-Study[18] and the Bogalusa Heart Study[28] underline that the prevention strategies and risk factor control should begin in childhood. The emphasis in the present thesis lied on non-invasive diagnostics of arterial structure (IMT) and its relation to health- and skill related physical fitness components. Sex- and age specific norm values for the IMT could be assessed for a German pediatric population[5] (Chapter 2). Additionally possible links between IMT, traditional cardiovascular risk factors, health- and skill-related physical fitness were investigated in healthy (Chapter 3), overweight and obese children and adolescents (Chapter 4).

Although no significant relations between health-related fitness and IMT could be demonstrated in healthy young children (Chapter 3), results in obese children demonstrated that physical fitness might play a role in correlation to arterial structure.
Obese children demonstrated impaired fitness and a thicker IMT in comparison to their normal weight peers (Chapter 4) and profited from a multidisciplinary, activity based intervention program (Chapter 5), by improving their IMT, as well as traditional cardiovascular risk factors and health- and skill-related physical fitness. Further in healthy primary school children 1.5 hours of basketball training once a week demonstrated only a slight effect on vascular structure. The IMT in the intervention group did not change whereas in the control group a significant increase could be demonstrated from baseline to the post examination 6 months later (Chapter 6).

To further elucidate the clinical relevance, the mechanisms linking arterial structure and function with physical fitness components need further investigation.

From the results of the present studies especially in obese children and adolescents it could be concluded that IMT as marker for the arterial structure is a “late” marker in the development of atherosclerosis, since pathological changes of the endothelium might take longer time to be positively influenced be interventions. In that context endothelial function might play an important role, stating that in the early development of atherosclerosis the endothelial function changes first, before a structural changes of the IMT follows. Therefore it could be suggested that future research should focus on arterial function, stiffness and compliance as well as endothelial function in correlation to physical fitness, exercise and physical activity.

It is further not understood, if exercise has a direct impact on the endothelium and arterial stiffness in the long run, but also immediately after a certain bound of exercise. It is still unclear, what kind of exercise and at what intensity level might have an effect on the vascular function. It could be suggested that due to exercising there might be a process of “vascular conditioning” due to the pressure induced stretching of the artery and shear stress.

It is also still unclear, if strategies that reduce risk factors in childhood, lead to an improvement in arterial structure and function in adolescents and adulthood.

However, it is unquestionable that health- and skill-related physical fitness components are fundamental for a healthy maturation of a child. Providing healthy, overweight and obese children and adolescents a chance to learn improve health- and skill-related fitness, to be able to learn and improve motor skills, is necessary for a meaningful involvement in physical activity and sport. By addressing the “first digital generation”[250] innovative approaches and networking of institutions and organizations[251] are essential to reduce inactive behaviors and to work towards the promotion of an active healthy lifestyle.

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