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STUDY OF ENDOTHELIAL FUNCTION IN ELITE ATHLETES OF DIFFERENT SPORTING DISCIPLINES COMPARED TO SEDENTARY CONTROLS

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Alle mie bambine, Violante e Lucrezia

I vostri sogni sono preziosi, custoditeli con coraggio

Inseguiteli con il cuore aperto

Perché i sogni si realizzano, al momento opportuno e nel modo migliore

Con immenso Amore, il vostro Papà

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1. Abstract

Introduction

Dyslipidemia is a major risk factor for atherosclerosis and cardiovascular diseases. Carotid intima-media thickness (IMT) and brachial flow-mediated dilation (FMD) are two recognized surrogates of early atherosclerotic changes and predictors of future CV events. Nowadays, no data on early vascular morpho-functional changes in dyslipidemic athletes are present. This study aimed to assess the relationship between lipid profiles and these early markers of vascular dysfunction and remodelling in Olympic athletes, compared to a sedentary control group.

Methods

A cohort of 388 athletes (57.2% males, mean age 29.5 ± 4.7 years old) was evaluated during pre-participation screening for the 2024 Olympic Games. Anthropometric data, blood samples for lipid profile and vascular assessments including carotid IMT and brachial artery FMD were collected. Dyslipidemia was defined as LDL ≥116 mg/dL. Athletes < 25 years or those taking anti-lipidemic drugs were excluded.

Results

Dyslipidemia was present in 96 athletes (24.7%), with a higher prevalence in males (29.3%) compared to females (18.7%). Endurance athletes exhibited a lower prevalence of dyslipidemia (14.5%) compared to mixed sports ones (31.2%). Dyslipidemic athletes had significantly higher IMT (0.62 ± 0.05 mm) compared to those with normal lipid profiles (0.57 ± 0.07 mm, $p<0.0001$), but no significant difference was observed in FMD between the groups ($p= 0.839$). Additionally, male athletes had higher IMT (0.59 ± 0.07 mm vs. 0.57 ± 0.06 mm, $p=0.004$) and lower FMD compared to females (12.3 ± 10.1% vs. 16.1 ± 11%, $p=0.0006$).

Conclusions

Our study revealed a high prevalence of dyslipidemia, particularly among male athletes and those engaged in mixed sporting disciplines. Conversely, endurance athletes displayed a

significantly lower prevalence of dyslipidemia, Moreover, we demonstrated an association between dyslipidemia and increased IMT (but not FMD) in both male and female athletes. These results emphasize the importance of regular dyslipidemia screening in elite athletes.

2. Introduction

2.1 Endothelium dysfunction

Endothelium is an active barrier between the vascular wall and the blood whom main functions are control of coagulation, fibrinolysis, vascular tone and immune response [1]. Under physiological conditions, endothelial cells exert vasodilatory, anti-inflammatory, anticoagulant, and antiproliferative effects, primarily through the release of mediators such as nitric oxide (NO) and prostacyclin. Endothelial dysfunction, especially impaired endothelium-dependent vasodilatation, refers to a shift in the endothelium toward a less favourable phenotype — diminished vasodilator and antithrombotic properties, increased proinflammatory, prothrombotic, and vasoconstrictive activity — has been linked to the pathogenesis of atherosclerotic vascular disease and acute cardiovascular (CV) events. Furthermore, this dysfunction occurs early before histological and angiographic evidence of arteriosclerosis[2].

Among the central mechanisms underlying endothelial dysfunction, impairment in NO bioavailability plays a critical role. NO, synthesized by endothelial nitric oxide synthase (eNOS) in response to shear stress, is essential for vasodilation, inhibition of platelet aggregation, suppression of smooth muscle cell proliferation, and reduction of leukocyte adhesion[3]. Decreased NO production can result from reduced eNOS expression or activity, deficiency of cofactors such as tetrahydrobiopterin (BH_4) and L-arginine, or increased NO degradation by reactive oxygen species (ROS). Notably, under conditions of oxidative stress or substrate deficiency, eNOS becomes "uncoupled," producing superoxide instead of NO and thereby further reducing NO bioavailability while amplifying oxidative stress[4]. Oxidative stress is a key determinant of endothelial dysfunction and derives from multiple enzymatic sources, including NADPH oxidases, uncoupled eNOS, xanthine oxidase, cyclooxygenases, lipoxygenases, and the mitochondrial respiratory chain[5]. Excess ROS rapidly react with NO to generate peroxynitrite, a highly reactive oxidant capable of damaging lipids, proteins, and

DNA, as well as oxidizing BH_4 and perpetuating eNOS uncoupling. In parallel, ROS activate redox-sensitive transcription factors such as NF-κB, which drive the expression of adhesion molecules, chemokines, and proinflammatory cytokines, fostering a self-perpetuating cycle of oxidative and inflammatory injury[6]. Inflammation constitutes another cornerstone of endothelial dysfunction. Proinflammatory cytokines such as TNF-α, IL-1β, and IL-6 upregulate adhesion molecules including VCAM-1, ICAM-1, and E-selectin, promoting leukocyte recruitment and transendothelial migration[7]. Activation of the NLRP3 inflammasome further amplifies this process by releasing IL-1β and IL-18, establishing a link between oxidative stress, innate immunity, and endothelial injury[8]. Chronic low-grade inflammation, typically associated with obesity, metabolic syndrome, and type 2 diabetes, creates a persistent hostile environment that impairs endothelial repair mechanisms and accelerates vascular aging[9]. Metabolic disturbances further exacerbate endothelial dysfunction: hyperglycemia promotes ROS generation, protein kinase C activation, and the formation of advanced glycation end-products (AGEs), which in turn impair NO signaling and amplify vascular inflammation[10]. Dyslipidemia contributes through the accumulation of oxidized low-density lipoprotein (ox-LDL), which activates endothelial cells, reduces NO, and triggers monocyte recruitment and foam cell formation[11]. In insulin resistance, the normal vasodilatory action of insulin via NO production is blunted, while hyperinsulinemia aggravates oxidative stress and inflammation, creating a deleterious cycle that promotes vascular injury[12]. Endothelial homeostasis also depends on reparative mechanisms such as endothelial progenitor cells (EPCs), which contribute to vascular repair. Their reduction in number or function, observed in diabetes, smoking, and aging, impairs endothelial regeneration[13]. Senescent endothelial cells, characterized by telomere shortening, DNA damage, and epigenetic alterations, adopt a proinflammatory and prothrombotic secretory phenotype that accelerates vascular dysfunction[14]. Moreover, dysfunction of anticoagulant pathways, including downregulation of thrombomodulin and upregulation of plasminogen

activator inhibitor-1 (PAI-1), shifts the homeostatic balance toward thrombosis, increasing the risk of acute vascular events[15]. Collectively, endothelial dysfunction emerges as a convergence point of mechanical, metabolic, oxidative, and inflammatory insults. These mechanisms interact in vicious cycles: oxidative stress reduces NO availability, which further impairs vasodilation and enhances inflammation; hypertension and disturbed flow amplify oxidative injury; and metabolic derangements both induce and are worsened by endothelial impairment. Such processes not only initiate but also sustain vascular remodeling, smooth muscle proliferation, extracellular matrix deposition, and arterial stiffening, thereby linking subclinical endothelial changes with clinical CV events[16].

From a clinical point of view, endothelial dysfunction represents both an early marker and a pathogenic mediator of CV disease. Its early onset, often preceding overt structural vascular changes, underscores its value as a prognostic indicator and therapeutic target. Because many of the underlying mechanisms—oxidative stress, inflammation, metabolic derangements, disturbed shear stress—are potentially reversible, interventions aimed at preserving or restoring endothelial function may have profound implications for the prevention and treatment of atherosclerosis and related CV disorders.

2.2 Diagnostic Techniques for the Assessment of Endothelial Dysfunction

The early detection of endothelial dysfunction is of paramount importance, as it represents a reversible stage in the continuum of CV disease progression. Since direct histological evaluation of the vascular wall is impractical in clinical settings, non-invasive surrogate markers have been developed to assess endothelial function and vascular remodeling: carotid intima media thickness (IMT) and flow mediated dilatation (FMD), measured by ultrasound are the most widely validated and extensively studied techniques, both important surrogate

markers of early atherosclerotic changes and predictors of future CV events [17,18]. Available data indicate that impaired FMD and increased IMT are associated with almost every condition predisposing to atherosclerosis and CV diseases, as a putative intermediate step for the development of subclinical target organ damage and later clinical events[19].

Flow-Mediated Dilation

FMD is a functional test that evaluates the ability of conduit arteries to dilate in response to increased shear stress, a physiological stimulus for NO release by endothelial cells. The technique is based on high-resolution ultrasound imaging of the brachial artery, usually performed in the antecubital fossa, to measure arterial diameter at baseline and after transient ischemia. Typically, a sphygmomanometer cuff is inflated on the forearm or upper arm to supra-systolic pressure (usually > 50 mmHg above systolic blood pressure) for about 5 minutes, inducing downstream ischemia. Upon cuff deflation, a rapid increase in blood flow occurs (reactive hyperemia), producing a surge in shear stress that stimulates NO-mediated vasodilation. The percentage increase in arterial diameter from baseline represents the FMD value, expressed as a percentage change.

FMD is considered the gold-standard non-invasive method for evaluating endothelium-dependent vasodilation. Importantly, pharmacological stimuli such as nitroglycerin can also be used to assess endothelium-independent vasodilation, thereby isolating the vascular smooth muscle response from the endothelial contribution. A reduced FMD indicates impaired endothelial NO bioavailability, reflecting early vascular dysfunction. Numerous studies have demonstrated that reduced FMD is associated with traditional CV risk factors such as hypertension, diabetes, smoking, dyslipidemia, and obesity, and that it predicts future CV events independently of conventional risk scores[20]. Despite its clinical value, FMD has limitations. The technique is highly operator-dependent, requiring meticulous attention to

image acquisition and analysis. Factors such as cuff placement (forearm vs. upper arm), duration of ischemia, time of measurement after cuff release, and even circadian variations can influence results. Furthermore, FMD requires standardization of protocols across laboratories to ensure reproducibility and comparability of findings. International guidelines have emphasized the need for rigorous methodological approaches, including fasting state, abstinence from caffeine and smoking before the test, and controlled environmental conditions[21]. Nevertheless, when properly conducted, FMD provides unique insights into endothelial function and remains a cornerstone technique in vascular research.

Carotid Intima-Media Thickness (IMT)

While FMD reflects the functional status of the endothelium, carotid IMT provides a structural measure of vascular remodeling and early atherosclerosis. IMT is assessed by high-resolution B-mode ultrasound of the common carotid artery, measuring the thickness of the intimal and medial layers of the arterial wall. Typically, measurements are performed in plaque-free segments of the far wall of the common carotid artery, about 1 cm proximal to the carotid bulb. The mean of several measurements, often bilaterally, is used as the IMT value, expressed in millimeters.

Increased IMT has been consistently associated with major CV risk factors, including age, hypertension, dyslipidemia, diabetes, and smoking. It correlates with the burden of subclinical atherosclerosis and has been shown to predict future CV events, including myocardial infarction and stroke [22,23]. Unlike FMD, which reflects endothelial dysfunction as an early and potentially reversible phenomenon, IMT represents structural vascular remodeling, capturing the cumulative impact of risk factors over time. Therefore, IMT is particularly useful for stratifying long-term CV risk and for assessing the efficacy of preventive interventions in longitudinal studies.

A major advantage of IMT is its reproducibility and ease of acquisition. Advances in ultrasound technology and automated edge-detection software have further improved measurement precision and reduced operator variability. Nevertheless, certain limitations remain. IMT is influenced by technical factors such as probe frequency, angle of insonation, and measurement site. Moreover, while increased IMT is associated with atherosclerosis, it does not necessarily reflect the presence of vulnerable plaques or lumen stenosis. For this reason, some guidelines recommend distinguishing between IMT measurement and direct assessment of carotid plaque, as both provide complementary information[24].

Complementary Roles of FMD and IMT

Although FMD and IMT evaluate different aspects of vascular health—functional and structural, respectively—they are complementary rather than competing techniques. Impaired FMD is often observed in the early stages of vascular disease, before structural changes become evident on IMT. Conversely, increased IMT reflects chronic exposure to risk factors and the progression toward overt atherosclerosis. Studies combining both measurements have shown that they provide additive prognostic information: reduced FMD identifies individuals at increased short-term CV risk, while increased IMT predicts long-term risk of clinical events[25]. From a pathophysiological standpoint, this distinction mirrors the natural history of atherosclerosis, in which functional impairment of endothelial cells precedes and accelerates structural arterial changes. Clinically, the combined use of FMD and IMT allows for a more comprehensive assessment of vascular health and may improve risk stratification beyond traditional factors. However, given the technical complexity of FMD, IMT has been more widely adopted in large epidemiological studies and clinical trials.

2.3 Lipid metabolism and dyslipidemia among elite athletes

Coronary heart disease and myocardial infarction are the leading cause of death in athletes

over 35 years old [26]. Lipids starts to deposit into the arteries since the young age, above all in persons with more CV risk factors. Cardiometabolic risk factors for diabetes mellitus and CV disease have been associated with CV morbidity and mortality in the general population and also in the past athletes[27]. Several reports found that young, active, and seemingly "healthy" professional athletes were not free of cardiometabolic risk, especially those with large body sizes[28,29]. Recently, high incidences of dyslipidemia, obesity, metabolic syndrome, and other CV risk factors were found in athletes[30-34] and in most of athletes cholesterol values above the threshold tends to persist over time[35]. Nowadays, studies evaluating the effects of dyslipidemia on early markers of atherosclerosis in élite athletes are lacking.

Physical exercise is a cornerstone intervention for improving lipid profiles and reducing CV risk in individuals with dyslipidemia. Numerous studies have shown that regular physical activity is associated with a reduction in LDL cholesterol and total cholesterol (TC), along with an increase in HDL cholesterol. These effects significantly contribute to the prevention of atherosclerosis and CV disease [36,37,38]. Aerobic exercise enhances lipid metabolism by increasing the activity of muscle lipoprotein lipase, thereby facilitating the catabolism of TG-rich lipoproteins [39].

Moreover, it reduces the activity of cholesteryl ester transfer protein (CETP), resulting in higher HDL concentrations. Among lipid parameters, HDL appears to be the most responsive to physical activity, with a clear association between increased exercise levels and both elevated HDL and lower TC values[39]. However, individual responses to exercise can vary based on coexisting and potentially confounding factors such as obesity, type 2 diabetes, or the use of lipid-lowering medications, which may modulate the lipid-related effects of physical activity[37,38]. Additionally, studies conducted in athlete populations have shown that, despite high training volumes, some athletes still exhibit lipid abnormalities—highlighting the possible role of genetic predisposition and other metabolic or lifestyle-related factors[34].

Guidelines recommend lowering LDL cholesterol concentrations to <100 mg/dL (2.5 mmol/L) for moderate-risk patients or to <70 mg/dL (<1.8 mmol/L) for high-risk patients[40]. Moreover, in primary prevention for individuals at very-high risk with familiar hypercholesterolemia (FH) and those without FH, an LDL-C reduction of at least 50% from baselined and an LDL-C goal of <55 mg/dL (<1.4 mmol/L) is reported, with class of recommendation IIa and I, respectively[40]. The first two targets usually does not apply within the specific context of elite athletes, who generally do not fall into high or very high CV risk categories. While HDL cholesterol has traditionally been viewed as "good cholesterol" due to its inverse relationship with CV risk, recent guidelines[40], including those from the ESC and European Atherosclerosis Society, do not recommend targeting HDL-C levels in lipid-lowering therapy. Instead, HDL is considered a secondary factor and should not be used alone for risk stratification.

To maximize exercise-induced benefits in individuals with dyslipidemia, moderate-intensity aerobic training remains the most widely recommended approach. Evidence supports that maintaining an energy expenditure >900 kcal/week and engaging in training sessions lasting over 40 minutes for at least 40 weeks can significantly improve the lipid profile, primarily by reducing LDL-C and TG. High-intensity interval training (HIIT) has shown promising results also in improving insulin sensitivity and reducing visceral fat, though its specific impact on lipid levels remains under investigation[38]. Additionally, incorporating resistance training with progressive overload may contribute to improved lipid metabolism and reduced systemic inflammation—key factors in managing CV risk[38]. When applied consistently and tailored to the individual, these exercise modalities serve as valuable non-pharmacological strategies to support lipid management and lower long-term CV risk.

Consistent with the American Heart Association (AHA) guidelines, the main CV risk factors for the general population include diet, physical activity, nicotine exposure, sleep health, body mass index, blood lipids, blood glucose, and blood pressure (BP)[41].

The 2013 update from the AHA using the National Health and Nutrition Examination (NHANES) data from 2007 to 2010 estimates that 9.1% of men and 6.7% of women aged 20 to 34 are hypertensive[42]. Vine M. et al. showed that among traditional CV risk factors in athletes, prior tobacco use was the most prevalent (40%), followed by a family history of atherosclerotic CV disease (21% in men, 17% in women), hypertension (17% in men, 13% in women), and dyslipidemia (10% in both men and women)[43].

However, a recent study conducted on 1,058 Olympic athletes (656 males, 402 females), consecutively evaluated between 2014 and 2016, yielded different findings. Dyslipidemia was identified as the most prevalent risk factor (32%), followed by increased waist circumference (25%), positive family history (18%), smoking (8%), hypertension (3.8%), and hyperglycemia (0.3%). A substantial proportion of athletes (n=418, 40%) presented with zero risk factors, while a similar proportion (414, 39%) exhibited only one risk factor. Conversely, a small subset (39, 3.7%) displayed three or four CV risk factors. An higher prevalence of endurance athletes was present in the risk-free group (34%)[36].

These findings support the observation that dyslipidemia and increased waist circumference are among the most common CV risk factors in elite athletes, with prevalence rates of 32% and 25%, respectively. A retrospective study enrolling 957 Olympic athletes (55.4% male, mean age 27.1±5 years, mean body mass index 23.1±3.2 kg/m²) showed that 343 athletes (35.8%) had dyslipidemia (LDL≥115 mg/dL or LDL/HDL≥1.90)[34].

Thus, despite their high levels of physical activity, studies have consistently shown that dyslipidemia ranks among the most prevalent CV risk factors in elite athletes, exceeding other traditional risk factors. These findings highlight the importance of routine screening and early intervention, even in seemingly low-risk, high-performance individuals.

In this setting, FH should be always taken into consideration as its prevalence is approximately 1 in 250 individuals in the general population and may be underrecognized among athletes, who often appear physically healthy and asymptomatic. Routine lipid

screening, including consideration of FH, is essential in athletic populations—particularly in those with a personal or family history of early CV events or persistently elevated LDL cholesterol despite lifestyle optimization. Indeed, it is recommended that a diagnosis of FH be considered in patients with coronary heart disease aged <55 years for men and <60 years for women; in individuals with relatives who experienced premature fatal or non-fatal CV death; in those with family members who have tendon xanthomas; in individuals with severely elevated LDL-C [>5 mmol/L (>190 mg/dL) in adults or >4 mmol/L (>150 mg/dL) in children]; and in first-degree relatives of patients diagnosed with FH [41]. Early identification through screening enables timely initiation of lipid-lowering therapy and lifestyle interventions, which are critical to reducing long-term CV risk. In athletic settings, heightened awareness among sports medicine professionals is essential to ensure that at-risk individuals are properly evaluated, regardless of their apparent health or physical fitness.

Although elite athletes are often perceived as having low CV disease risk, recent evidence suggests that both Olympic and Paralympic athletes (PAs) exhibit a significant burden of CV risk factors, particularly dyslipidemia[36,44,45]. Cholesterol variation across different athlete subgroups is reported in **Table 1**.

A retrospective analysis of screening data from 289 athletes who participated in the Paralympic Games between London 2012 and Beijing 2022 was conducted in 2023 to estimate the prevalence of dyslipidemia. The cohort was stratified according to sport discipline and disability classification, specifically spinal cord injury (SCI) and non-spinal cord injury (NSCI). The prevalence of dyslipidemia was identified as the most frequent CV risk factor within this population, affecting 35% of the athletes. Longitudinal assessment revealed only mild changes in lipid profiles over the medium-term. Stratified analysis indicated a significant association between disability type and sporting discipline (i.e. power, skill, and mixed) with lipid parameters, demonstrating improvements in HDL and reductions

in LDL. Notably, a more favourable lipid profile was observed in athletes participating in endurance disciplines[44].

Endurance athletes with NSCI, compared with those with SCI, featured higher HDL (68.1±17 mg/dL vs 60.6±10.9 mg/dL, p=0.04) and, even if not statistically significant, lower LDL (97.9±27.4 mg/dL vs 104.1±30.6 mg/dL, p=0.38), with similar TC levels (70.2±25.9 mg/dL vs. 71.2±20.7 mg/dL, p=0.87).[44]

A follow-up study on 99 master PAs (aged ≥40 years) revealed an even higher dyslipidemia prevalence (54%) and identified 30% of athletes as having high or very-high CV risk, according to the European Society of Cardiology – Systematic Coronary Risk Evaluation 2 (ESC-SCORE2)[45]. Notably, despite prolonged lipid abnormalities, none of the affected athletes received pharmacological treatment, and dyslipidemia remained largely untreated.

These findings highlight the need for targeted screening and preventive strategies in PAs populations, emphasizing the importance of early intervention to mitigate long-term CV risk. The persistently high prevalence of dyslipidemia, despite athletic training, underscores the need for structured CV monitoring, particularly in PAs with SCI and those engaged in non-endurance sports[45].

The observed differences in lipid profiles between Olympic and PAs may be related to several physiological and lifestyle factors. One possible hypothesis is that PAs, particularly those with SCI, experience altered lipid metabolism due to reduced muscle mass and autonomic dysfunction[46]. This may impair lipid clearance and increase LDL levels while lowering HDL. Additionally, mobility limitations could lead to reduced overall energy expenditure, impacting lipid regulation despite participation in elite sports. Another hypothesis focuses on training regimes. Indeed, PAs might have reduced engagement in endurance training, which is known to positively influence lipid profiles by increasing HDL and lowering TG. Furthermore, a

chronic inflammatory state associated with certain disabilities may contribute to dyslipidemia by altering lipid metabolism and promoting atherosclerotic processes[47,48]

Based on the above described evidences, the aim of the study was to investigate in a cohort of Italian elite athletes, practicing different sporting disciplines, the correlation between lipid profile and early markers of atherosclerosis (i.e. endothelial dysfunction and vascular remodeling) in order to identify clinical characteristics of those at high risk for the development of atherosclerotic disease and possible future clinical cardiac adverse events, comparing also to a sedentary age and gender matched control group.

3. Materials and Methods

The study design of the present investigation was evaluated and approved by the Ethic Committee Lazio Area 1 (date of approval 06/03/2024; IRB approval code: 0208/2024). All athletes included in this study were fully informed of the types and nature of the evaluation and signed the consent form, according to Italian Law. All clinical data collected from the study population are stored in an institutional database. The work described was performed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

In our study we included a large cohort of 394 Olympic athletes evaluated during pre-participation screening for 2024 Paris Olympic Games. All were world-level competitors, and a substantial proportion (39%) had participated in more than one Olympic Game. Athletes < 25 years or those taking either statins, ezetimibe or supplements with anti-lipidic actions (n=3) and females athletes with amenorrhea (n=3) were excluded from the study: the final cohort comprised a total of 388 athletes. Moreover, we've enrolled an age-matched control group of 100 sedentary persons (50 males and 50 females), not meeting the recommended levels of physical activity. A blood test sample was collected and the following biochemical

indices were analyzed: total cholesterol (TC), low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, triglycerides (TG) and liver function enzymes: aspartate aminotransferase (AST) and alanine aminotransferase (ALT), thyroid stimulating hormone (TSH), free triiodothyronine (FT3) and free thyroxine (FT4).

Blood samples were collected early in the morning and after at least 10 hours fasting and were analyzed on the same day. All blood tests were collected and analyzed into the same laboratory.

Blood pressure was recorded in the sitting position before exercise testing, as recommended[49]

Athletes were engaged in a wide spectrum of sport disciplines, classified into four groups, as previously described[50]

1) power (strength disciplines): weightlifting, Greco-Roman wrestling, judo, javelin, shot-putting, swimming (<800 mt), athletics (sprinting, shot putting and discus).

2) skills (technical disciplines): archery, equestrian, golf, shooting, sailing, diving, equestrian sports.

3) endurance (primarily dynamic components): cycling, rowing, canoeing, triathlon, long-distance running, long-distance swimming (>800 mt), pentathlon, biathlon.

4) mixed disciplines (alternate dynamic and strength components): soccer, volleyball, basketball, tennis, fencing, water polo, rhythmic gymnastics, taekwondo, badminton, beach volley, softball.

Body height and weight were obtained in each subject and body mass index (BMI) was calculated as weight (kg)/height (m)2. Body composition and fat mass percentage measurement was made with Bioelectric Impedance Analysis (BIA 101 Quantum, Akern, Italy), with constant sinusoidal current, at an intensity of 50 kHz and 400 μA. In athletes, dietary assessment aimed to quantify total energy intake, macronutrient and micronutrient intake, and/or to estimate the adequacy of the diet in terms of specific nutrient consumption and timing of intake during training or competition.

We used a retrospective dietary assessment with the collection of diet history: an interview during which the athlete is asked to provide details about their overall eating habits and to describe a typical day\week[51]. The dietary surveys were then processed using the Keyson software, which enables a qualitative and quantitative estimation of dietary data (with % of fat, proteins and carbohydrates) (Keyson | Software per professionisti della nutrizione, Keyson SRL, Monteprandone, AP, Italy)"

3.1 Assessment of Cardiovascular Risk Factors

CV risk factors were defined as follow:

- Family history for cardiovascular disease: fatal or non-fatal CV events or/and established diagnosis of CV disease in first-degree male relatives before 55 years, or female relatives before 65 years[52] or evidence of carotid\peripheral atherosclerotic disease in first degree relatives[53];
- Family history for dyslipidemia: first-degree relative in treatment (pharmacological or nutraceutical);
- Cigarette smoking: defined as regularly smokers of at least one cigarette per day[52];
- Overweight: body mass index (BMI) over 25; obesity: BMI over 30[52];
- Dyslipidemia: was defined as LDL ≥ 116 mg/dL (12,19,20); HDL < 40 mg/dL for males or HDL < 50 mg/dL for females, Hypertriglyceridemia: TG values superior to 150 mg/dl[54]

3.2 Flow mediated dilation procedure

FMD assessment of the brachial artery was evaluated by using a high-resolution vascular ultrasound (10 MHz transducer, attached to a GE Vivid E9, GE Healthcare or Philips EPIQ 7Q 5 echographs) by a single expert sport Cardiologist (GDG), specialized in cardiac and vascular echography.

Vascular response to reactive hyperemia in the brachial artery was used for assessment of endothelium-dependent FMD. After resting in supine position for 10 minutes, internal diameter of the brachial artery is assessed at the end of diastole (timed by the QRS complex). A cuff fitted 8 cm distal to the brachial artery and near the wrist is inflated up to 250 mmHg for 5 minutes. When the clearest B-mode image of the anterior and posterior intimal interfaces between the lumen and vessel wall was obtained, the transducer was held at the same point throughout the scan and measure of brachial artery diameter acquired (**Figure 1, Panel A**). Depth and gain setting were set to optimize the images of the arterial lumen wall interface.

After deflating the pneumatic forearm cuff, the vessel's maximal diameter is determined again at the same point as for the resting measurement (diameter during reactive hyperemia) at 15 seconds and 45 to 60 seconds (**Figure 1, Panel B**). Diameter changes are derived as percent change relative to the first (baseline) scan. Thus, FMD equals: [(diameter after cuff deflation – resting diameter)/resting diameter x 100][55]

Before each measurement, the participants rested in a supine position for 15 min with their right arms extended < 80° laterally from the torso and at the heart level, in a quiet climate control room (22-24°C). Optimal cut-off values of FMD used in our study, early validated for subjects with no CV disease, was 7.1%[56].

3.3 Carotid ultrasound assessment

Carotid IMT was measured using similar equipment as that used for FMD. Scanning included the left and right carotid arteries, as previously described (**Figure 2**)[57].

The carotid artery image were focused on the far wall and 3 segments were identified on each side: (i) common carotid artery (defined as the segment 1 cm proximal to carotid dilatation); (ii) carotid bulb (defined as the segment between the carotid dilatation and carotid flow divider); and (iii) internal carotid artery (defined as the 1 cm long arterial segment distal to the flow divider). In each segment three measurements of the maximal carotid IMT in the far

wall were averaged. Subsequently, the average maximal carotid IMT of all 6 segments were calculated as the mean carotid IMT.

4. Statistical analysis

Sample size calculation

The sample size was calculated to estimate the prevalence of dyslipidemia among athletes. Based on previous literature, an expected prevalence of 28% was assumed.

Using the standard formula for proportions, with a 95% confidence level (Z = 1.96) and setting the margin of error to yield a sample size of approximately 400 subjects, we obtained:

$n = [Z^2 \, p \, (1-p)]/e^2$

Where:

- p = 0.28 (expected prevalence),
- 1−p = 0.72
- Z = 1.96
- e ≈ 0.044 (corresponding to a margin of error of about 4.4%).

Step by step:

1. $Z^2 = 3.8416$
2. $p \, (1-p) = 0.2016$
3. $3.8416 \times 0.2016 = 0.7747$
4. $n = 0.7747/0.044^2 \approx 400$

A total of 400 athletes have been enrolled, of whom approximately 112 were expected to be dyslipidemic and 288 with normal lipid profile. In addition, 100 sedentary controls (50 male), aged 25–40 years, have been recruited for external comparison.

Categorical variables were expressed as frequencies and percentages and were compared using Fisher's exact test or Chi-square test, as appropriate. Normality criteria were checked for any continuous variable, which was presented as mean and standard deviation (SD) and compared using the Student t-test for independent data if normally distributed. Pearson's correlation coefficient was used for correlation analysis. The comparative analysis between the different types of sports was performed using the Dunn test and Pairwise comparison method. The tables show the pooled p-value [of the comparison test with the 4 categories: P (power), S (skill), E (endurance), and M (mixed)]. If pooled $p < 0.05$, a pairwise test was performed. All pairwise tests were considered significant if $p < 0.05$. Statistical analysis was performed with STATA Statistics for Windows (SE, version 17) software.

5. Results

5.1 Overall Population

We enrolled 388 Olympic athletes (222 males, 57.2%), mean age 29.5 ± 4.7 years old, mean BMI 23.2 ± 2.8 kg/m^2, practicing different sporting disciplines divided as follow: skill 86 (22.2%), power 104 (26.8%), endurance 110 (28.4%) and mixed 89 (22.9%). Most of the athletes were Caucasians (371, 95.6%); eighty-two athletes (21.1%) had a BMI over 25 kg/m^2, while 7 (1.8%) overcome 30 kg/m^2. Active smoking was reported in 10.6% of the athletes (n=41), while 26.8% had a family history for cardiovascular disease (n=104) and 10.6% (n=35) at least one of the parents with dyslipidemia.

As control group, we've enrolled 100 sedentary subjects (50 males and 50 females), mean age 30.8 ± 6.6 years old, mean BMI 24.2 ± 3.1 kg/m^2, with 39 with BMI > 25 kg/m^2 and 7

with grade I obesity. All controls were Caucasians. Twenty-four subjects were active smokers, 36 had familiarity for cardiovascular diseases and 16 for dyslipidemia.

Globally, no clinically or statistically differences in age were present between the two groups (p=0.089), with control group presenting higher BMI (p=0.002), subsequently an higher prevalence of overweight subjects (p=0.0002) and obesity prevalence (p=0.005). Moreover, an higher prevalence of smokers were noted in sedentary group (p=0.004), while similar rates of familiarity for cardiovascular disease (p=0.071) and dyslipidemia (p=0.064) were present.

5.2 Dyslipidemia

In our cohort 96 athletes (24.7%) were dyslipidemic **(Figure 3)**; the most common altered value was LDL-cholesterol: more specifically, 79 (20.4%) had LDL-C above the threshold; 70 of them with isolated elevated LDL; in 5 athletes (2 females and 3 males) an hypo-HDL was associated and in 4 athletes an hypertriglyceridemia was present. Moreover, 16 athletes (4.1%) had hypo-HDL cholesterol levels (5 females); in one athlete an hypertriglyceridemia was co-existent, in 10 an isolated hypo-HDL-C was identified. Finally, hypertriglyceridemia was detected In 11 (2.8%) athletes; only 6 cases were isolated and not combined with other cholesterol abnormalities.

In control group, 37 subjects had altered lipidic values; all the sedentary subjects presented altered LDL values, 2 males having also hypertriglyceridemia and 1 male with hypo-HDL.

In **Table 2** are listed main differences between dyslipidemic athletes and those with normal lipid profile. Dyslipidemic athletes had similar age (30.2 ± 5.5 years vs. 29.3 ± 4.3 years, p=0.126) compared to those with normal lipid profile, but a higher prevalence of male athletes was present (67.7% vs. 53.8%, p=0.016). A similar prevalence of athletes with familiarity with dyslipidemia was recorded between athletes with normal lipid profile (9.9%) and those with dyslipidemia (6.3%, p=0.275), as well as in the sedentary control group (15.9%) in those with normal lipid profile, compared to 16.2% of dyslipidemic (p=0.964), with a statistical

value close to significance (p=0.073) in the comparison between the two dyslipidemic population.

Then, significant differences in anthropometric parameters were found, with those with altered lipid profile showing higher BSA (p=0.0006), greater weight (p=0.0007), higher BMI (p=0.003) and overweight prevalence (30.2% vs. 18.2%, p=0.012) and greater waist circumference (WC) (80.2 ± 8.7 cm vs. 76.8 ± 7.5 cm, p=0.0003) and similar fat mass % (p=0.652). Then, athletes with a normal lipid profile and those with dyslipidemia showed comparable dietary fat intake (30.5 ± 4.4 vs. 30.8 ± 4.6, p=0.602), as well as similar protein (p=0.198) and carbohydrate intake (p=0.162). When comparing thyroid function parameters between athletes with a normal lipid profile (n = 292) and those with dyslipidemia (n = 96), no statistically significant differences were observed. Serum FT3 levels were 4.86 ± 1.3 pg/mL in the normal lipid profile group and 5.03 ± 1.1 pg/mL in the dyslipidemic group (p = 0.21). FT4 values were 15.4 ± 4.8 pmol/L and 15.6 ± 2.8 pmol/L, respectively (p = 0.62). TSH concentrations were slightly higher in dyslipidemic athletes (2.17 ± 0.94 mIU/L) compared with those with normal lipid profiles (1.97 ± 1.1 mIU/L), but this difference did not reach statistical significance (p = 0.085).

Also sporting disciplines significantly affected lipid profile, with lower prevalence of dyslipidemic athletes in endurance disciplines (19% vs. 31%, p=0.016) and an higher prevalence observed in mixed sports (31.2% vs. 20.2%, p=0.025).

Finally, in control group, dyslipidemic subjects were more frequently male (78.4% vs. 33.3%, p<0.0001), with subsequently constitutional differences gender-related: taller (p=0.0001), heavier (p<0.0001) and with an higher BMI (p<0.0001). At blood tests results, all lipid profile parameters were significantly higher: TC (p<0.0001), LDL (p<0.00001) and TG (p=0.001), with lower HDL (p=0.0009).

5.3 Endothelial dysfunction analysis

Significant differences in vascular morphological parameters were found, with different IMT between dyslipidemic athletes (0.62 ± 0.05 mm) and those with normal lipid profile (0.57 ± 0.07 mm in, p<0.0001). No differences were found in functional vascular parameters, with similar FMD% (p=0.839) and similar prevalence of reduced FMD (p=0.882).

Moreover, dyslipidemic sedentary subjects presented higher IMT (0.64 ± 0.05 mm vs. 0.56 ± 0.05 mm, p<0.0001), larger brachial artery diameter (BAD) (p=0.001) and lower values of FMD (12.4 ± 9.3% vs. 19.8 ± 10.7%, p=0.0008) with higher (but not statistically significant) prevalence of low FMD (27% vs. 12.7%, p=0.073).

The comparison between the two dyslipidemic population showed that sedentary subjects presented a higher prevalence (37% vs. 24.7%, p=0.014), a higher prevalence of overweight subjects (54.1% vs. 30.2%, p=0.010), with similar values of serum lipid components, but higher IMT in sedentary control group (0.64 ± 0.05 mm vs. 0.62 ± 0.05 mm, p=0.005), with similar values of vascular artery dimension parameters and function.

Finally, focal thickening of carotid vessels were found in 2 males dyslipidemic athletes (**Figure 4, Panel A and B**) and in 2 male sedentary subjects (**Figure 4, Panel C and D**).

In athletes population, a significant positive correlation was found at linear simple regression analysis (**Figure 5**) between IMT and LDL cholesterol (p<0.0001; R^2=0.08) (**Figure 5, Panel A**), with an inverse statistical borderline correlation with HDL cholesterol (**Figure 5, Panel B**) (p=0.07; R^2=0.007) and consequently, a significant correlation with LDL/HDL ratio (**Figure 5, Panel C**) (p<0.0001; R^2=0.05). Finally, no correlation between the carotid parameter and TG was found (**Figure 5, Panel D**) (p=0.465; R^2=0.001).

Moreover, concrete differences were found in correlation between IMT and normality\elevated LDL cholesterol. In fact, in athletes with elevated serum LDL cholesterol, a significant positive correlation was highlighted at simple linear regression analysis (**Figure 6, Panel A**) (p=0.0006; R^2=0.11). On the other hand, no association was found in those with normal LDL values (**Figure 6, Panel B**) (p=0.357, R^2=0.002).

5.4 Gender influence

Several significant gender differences in athletes population were highlighted. As shown in **Table 3**, males presented higher anthropometric parameters with larger BSA ($p<0.0001$), body weight and BMI ($p<0.0001$), prevalence of overweight (27.9% vs. 12% in female athletes, $p=0.0001$), lower body fat mass % (11.1 ± 4.9% vs. 19.7 ± 5.2%, $p<0.0001$). Despite the higher prevalence of males athletes practicing endurance disciplines, compared to females (32.4% vs. 22.9%, $p=0.039$), males had a worst lipid profile characterized by higher LDL cholesterol (100.6 ± 27.1 mg/dL vs. 93.7 ± 24 mg/dL, $p=0.009$), lower HDL (61.3 ± 15.3 mg/dL vs. 74.2 ± 14.5 mg/dL in females, $p<0.0001$) and higher TG (78.2 ± 39.8 mg/dL vs. 68.6 ± 26.1 mg/dL, $p=0.006$).

Additionally, significant gender differences in morphological and functional vascular parameters were found. In fact, males had thick carotid intima media (0.59 ± 0.07 mm vs. 0.57 ± 0.06 mm, $p=0.004$), lower FMD % (12.3 ± 10.1% vs. 16.1 ± 11%, $p=0.0006$) and higher prevalence of low FMD (26.1% vs. 17.5%, $p=0.043$) compared to female athletes counterpart.

Dyslipidemia was significantly more frequent in male athletes (65\222, 29.3%) compared to females (31\166, 18.7%, $p=0.016$).

Dyslipidemic male athletes presented larger anthropometric features compared to males with normal lipid profile characterized by larger BSA ($p=0.009$), body weight ($p=0.005$) and BMI ($p=0.0008$), with also higher % of body fat mass ($p=0.045$) and larger WC ($p=0.0006$). In males with altered lipid profile a lower prevalence of those practicing endurance disciplines was reported (16.9% vs. 38.9% , $p=0.001$). On the other hand, an higher prevalence of mixed sports was noted (32.3% vs. 17.2%, $p=0.012$). Additionally, in dyslipidemic male athletes a significantly thicker carotid IMT was measured (0.62 ± 0.05 mm vs. 0.58 ± 0.06 mm,

p<0.0001), but similar vascular functional parameters, with similar FMD (12.9 ± 10.8% vs. 12 ± 9.7%, p=0.541) and similar prevalence of low FMD (p=0.995).

In female athletes, no significant differences in anthropometric parameters were found between dyslipidemic and those with normal lipid profile. Moreover, no prevalent sporting category was found in females with altered lipid profile. Therefore, in lipid profile similar HDL cholesterol levels were found between the dyslipidemic and those with the normal lipid profile. Finally, as well as in male counterpart also in females athletes an higher IMT was measured (0.60 ± 0.04 mm vs. 0.57 ± 0.06 mm , p=0.016). Functional vascular parameters were similar between the two groups also in female athletes (FMD: 16.2 ± 12.9% vs. 16 ± 10.5% in normal lipids, p=0.926 and FMD < 7.1%: 16.1% vs. 17.8%, p=0.761).

5.5 Sporting categories

According to the last ESC classification, athletes were divided into four groups: skill (n=86, 22.2%), power (n=104, 26.8%), mixed (n=89, 22.9%) and endurance (n=110, 28.3%). Significant differences were found in diet between the different categories (**Table 4**), with endurance athletes assuming the lowest fat % (p=0.0007) and the highest carbohydrate doses (p=0.019) with no differences in protein intake (p=0.921). On the other side, athletes practicing skills disciplines assumed the highest fat intake and the lowest carbohydrate quantities.

Similar rates of dyslipidemic athletes in different sporting categories were highlighted (p=0.150) , with endurance presenting the lowest prevalence (14.5%) and skills athletes the highest (26.7%). On those basis, significant differences in serum lipid concentrations were measured with endurance athletes having the lowest LDL cholesterol (p=0.028), the highest HDL (p=0.003) and consequently the lowest LDL/HDL ratio (p=0.005) and the lowest serum TG concentrations (p<0.0001).

The evaluation of vascular morphological and functional parameters demonstrated that endurance athletes had the largest brachial artery diameter ($p<0.0001$) as well as the lowest FMD % ($p=0.0001$) and the highest prevalence (32.7%) of reduced FMD ($p=0.023$).

6. Discussion

Our study investigated in a large cohort of Italian elite athletes the association between lipid profile and early markers of atherosclerosis such as endothelial dysfunction and vascular remodeling in order to identify clinical characteristics of those at high risk for the development of atherosclerotic disease and possible future clinical cardiac adverse events.

6.1 Prevalence of dyslipidemia

Dyslipidemia represents one of the most relevant cardiovascular risk factors worldwide, being directly associated with the development and progression of atherosclerotic cardiovascular disease[58,59]. In our study, we found that almost one out of four elite athletes (24.7%) presented an altered lipid profile. This prevalence appears remarkably high when considering that our population was relatively young (mean age below 30 years) and engaged in regular high-intensity physical activity, which is usually associated with favorable lipid metabolism and cardioprotective effects[60]. The prevalence observed in our study is similar to that reported in some general populations of comparable age groups[61], but it remains surprising for an elite athletic cohort, in whom lifestyle, dietary habits, and regular structured training should theoretically mitigate the risk of lipid abnormalities.

The predominant abnormality detected was elevated LDL cholesterol, affecting approximately 20% of the athletes. Elevated LDL-C plays a central role in the initiation and progression of atherosclerosis[62], and our results suggest that athletic training per se does not uniformly protect against this abnormality. Interestingly, hypo-HDL and

hypertriglyceridemia were relatively uncommon among athletes, which might reflect the protective effect of regular exercise on HDL metabolism and TG clearance[62]. Nonetheless, the presence of hypo-HDL, especially in female athletes, raises concerns given the established role of HDL in reverse cholesterol transport and vascular protection[62].

The relatively high prevalence of dyslipidemia among elite athletes suggests that other factors beyond physical training contribute to lipid abnormalities. Genetic predisposition, diet composition, body composition differences, and the specific physiological demands of different sporting disciplines may all play a role[58,60]. Furthermore, our findings underscore the importance of considering cardiovascular screening programs also in elite athletes, rather than assuming a uniformly favorable cardiometabolic profile in this population.

6.2 Vascular implications

Our study provides important insights into the vascular consequences of dyslipidemia in elite athletes. Dyslipidemic athletes showed significantly higher carotid IMT compared to those with normal lipid profiles, irrespective of gender. Increased IMT is a recognized marker of subclinical atherosclerosis and is predictive of future CV events[62,63]. The presence of carotid focal thickening in some dyslipidemic athletes further strengthens the evidence of early vascular remodeling in this group.

Interestingly, functional vascular parameters, particularly FMD, were not significantly different between dyslipidemic and non-dyslipidemic athletes. This contrasts with sedentary dyslipidemic individuals, where FMD was significantly impaired[63]. One possible explanation is that the high level of physical activity in athletes may preserve endothelial function despite structural remodeling of the arterial wall. Shear stress induced by exercise is known to enhance NO bioavailability and endothelial resilience, which could act as compensatory mechanisms counterbalancing the adverse effects of dyslipidemia. Thus, vascular remodeling

(as evidenced by increased IMT) may precede functional impairment (reduced FMD) in athletes, suggesting a distinct temporal pattern of vascular changes in this highly trained population.

Another key finding is that endurance athletes, despite their favorable lipid profile, exhibited the lowest FMD values and the highest prevalence of reduced FMD. This apparent paradox may be explained by the larger baseline BAD observed in endurance athletes, which could reduce the relative percent increase in diameter during FMD testing. The relationship between vessel size, shear stress, and endothelial responsiveness is complex, and in endurance athletes, chronic adaptations may result in structural enlargement that alters the interpretation of FMD values without necessarily indicating impaired endothelial function.

6.3 Gender differences

One of the key observations in our study is the significant influence of gender on lipid profile and vascular health among athletes. Male athletes were not only more frequently dyslipidemic than females (29.3% vs. 18.7%) but also displayed a more atherogenic lipid profile characterized by higher LDL cholesterol, lower HDL cholesterol, and higher TG. These findings are consistent with prior studies demonstrating that premenopausal women generally present more favorable lipid profiles compared to men, due to the protective role of estrogens on lipid metabolism and vascular function[63,64].

In terms of vascular parameters, males showed thicker carotid intima-media thickness (IMT), lower flow-mediated dilation (FMD), and a higher prevalence of impaired endothelial function compared to female athletes. This is particularly relevant because increased IMT and reduced FMD are independent predictors of future cardiovascular events[62,63]. The combination of adverse lipid profiles and vascular remodeling observed in male athletes may indicate a higher long-term CV risk, even in the presence of intense physical training.

Interestingly, in female athletes the presence of dyslipidemia was not associated with significant changes in anthropometric parameters or training categories. Conversely, in males, dyslipidemia was clearly linked with larger body size, higher BMI, increased WC, and higher fat mass percentage, as well as a lower prevalence of endurance sports participation. This suggests that body composition and sport-specific training regimens interact differently with lipid metabolism depending on gender[61,63].

Taken together, these findings highlight that male athletes remain at higher risk of vascular remodeling and adverse lipid profiles despite high training volumes, and gender-specific preventive strategies should be considered.

6.4 Sport-specific effects

When analyzing lipid profiles across different categories of sports, important differences emerged. Endurance athletes consistently showed the most favorable lipid profile, with the lowest LDL cholesterol, highest HDL cholesterol, lowest TG, and consequently the most advantageous LDL/HDL ratio. Conversely, athletes participating in skill-based disciplines showed the worst lipid parameters, whereas those in mixed sports had the highest prevalence of dyslipidemia. These findings reinforce the notion that the type of training plays a crucial role in shaping lipid metabolism[58].

Aerobic endurance training is known to improve lipid metabolism through several mechanisms, including increased lipoprotein lipase activity, enhanced TG-rich lipoprotein clearance, and improved cholesterol efflux capacity[58,60]. Previous studies have demonstrated that regular aerobic activity raises HDL cholesterol and reduces LDL cholesterol concentrations, ultimately lowering CV risk[60]. Our results confirm these effects in a large cohort of elite endurance athletes, supporting the cardioprotective nature of aerobic-based training.

In contrast, skill sports are often characterized by lower overall training volumes and intermittent, less metabolically demanding efforts. This may explain the less favorable lipid profile observed in this category, as the cardiometabolic impact of skill-based training is less pronounced compared to endurance exercise. Power and mixed sports, which combine strength and variable aerobic demands, showed intermediate profiles, but with a notably higher prevalence of dyslipidemia in mixed disciplines. This may reflect the heterogeneous nature of these sports, which often require higher body mass and involve substantial anaerobic effort, potentially counteracting some of the lipid-improving effects of aerobic training[60].

Another intriguing observation is that dietary habits significantly differed among the categories, with endurance athletes consuming the lowest fat and the highest carbohydrate intake. These nutritional patterns are consistent with current sports nutrition guidelines for endurance disciplines[58] and may contribute to their more favorable lipid profile. Conversely, higher fat intake observed in skill athletes may partially explain their higher dyslipidemia rates. These findings underscore the interaction between training modality, diet, and lipid metabolism in shaping CV risk among athletes.

6.5 Comparison with sedentary controls

The comparison between athletes and sedentary individuals provided further valuable insights. Dyslipidemia was more prevalent among sedentary subjects (37% vs. 24.7%), and it was associated with more pronounced alterations in lipid values, thicker IMT, and impaired FMD. These findings confirm the protective role of physical activity on vascular health and lipid metabolism, even in the presence of dyslipidemia[65]. In fact, while dyslipidemic athletes showed increased IMT, their FMD remained preserved, whereas sedentary dyslipidemic individuals already displayed both structural and functional vascular impairments[66,67].

This suggests that high-level physical training may attenuate, but not fully eliminate, the vascular consequences of dyslipidemia. Athletes with altered lipid profiles still develop signs

of vascular remodeling, but the preservation of endothelial function might delay the onset of clinically relevant vascular disease. Conversely, sedentary individuals experience a more rapid transition from dyslipidemia to both structural and functional vascular impairment, potentially accelerating the progression to overt cardiovascular disease[65,66,68].

Taken together, these observations emphasize that elite athletes are not immune from dyslipidemia and its vascular consequences, but their high training levels may confer a partial protective effect. This highlights the importance of regular CV screening also in the athletic population, as dyslipidemia in athletes may remain clinically silent but still lead to subclinical vascular changes detectable at carotid ultrasound.

Finally, a comparison between study results and literature findings on dyslipidemia, vascular function, and sport-specific effects is shown in **Table 5**.

7. Limitations

Our study has several limitations. Main limit in preventive studies trying to identify and early treat high-risk young population is lack of concrete outcome data (CV events), so randomized or retrospective studies miss their strength for two practical reasons. First, since event rates are much smaller in young individuals, the number of participants to be enrolled would be in the tens of thousands. Second, the study costs would be exorbitant. A 25-30-year prevention trial based on future development of CV clinical events in a general population will likely never be realized, moreover in selected population like elite athletes.

Most importantly, the irrefutable results of statin intervention trials, in the general population and in sub-population studied, leave no doubt that reducing LDL cholesterol levels reduces overall CV risks; this hypothesis is strongly supported from epidemiologic correlations, pathologic observations, mechanistic studies and animal model studies[32,33].

Other limitation is represented by the demographic characteristics of the analyzed population: small age range (most of them under 30 years old), large sample but still limited to a single

center, it includes mainly Caucasians and athletes of exclusively Italian nationality, limiting generalizability.

Hence, upcoming prospective studies are required to validate the proposed theories and to evaluate its prognostic impact on CV health.

8. Future perspective

The findings of our study open several avenues for future research that deserve careful exploration. First, it will be crucial to design large, prospective longitudinal studies to better assess the actual impact of lipid alterations on CV risk in elite athletes. Such studies should include long-term follow-up to evaluate the evolution of subclinical markers of atherosclerosis, such as carotid IMT, and their association with major clinical events. A longitudinal approach would also clarify whether the vascular changes observed in our cohort represent a transient phenomenon linked to the competitive phase of an athletic career or whether they persist over time, potentially contributing to an increased CV risk after retirement, when physical activity levels typically decline.

Another important future direction involves the evaluation of targeted therapeutic strategies for the early management of dyslipidemia in athletes. In this regard, upcoming studies should compare the efficacy of pharmacological treatments (statins, ezetimibe, PCSK9 inhibitors) with non-pharmacological approaches, such as nutraceutical supplementation (e.g., phytosterols, omega-3 fatty acids, red yeast rice), dietary modifications, and personalized training programs. Considering the relatively young age of this population, as well as their high sensitivity to issues related to performance and recovery, it will be crucial to assess the safety of these interventions and their potential influence on athletic performance, muscle recovery, and overall training capacity.

Gender differences also deserve further attention. Our data showed a worse lipid profile in male athletes, associated with higher IMT values and reduced endothelial function compared to females. Future studies should aim to elucidate the biological and hormonal mechanisms underlying these differences and investigate whether female athletes are truly protected or if this apparent advantage diminishes with age or after retirement. It will also be relevant to examine whether gender-specific training protocols may modulate lipid profiles and vascular parameters differently.

The type of sporting discipline is another determinant that requires deeper investigation. Our results indicated that endurance athletes displayed a more favorable lipid profile and a lower prevalence of dyslipidemia, whereas athletes engaged in mixed sports appeared more exposed. Future research should clarify the pathophysiological mechanisms behind these differences, integrating advanced body composition analyses (e.g., MRI, DEXA) and metabolic studies of lipid utilization during and after exercise. This may help determine whether prolonged aerobic training has a genuine protective effect on lipid metabolism and vascular health, independent of diet and body composition, or if the observed differences are largely due to confounding factors such as dietary patterns, fat mass percentage, or genetic predisposition.

Moreover, expanding study cohorts to include athletes from different ethnic backgrounds and geographical areas will be fundamental to evaluating the generalizability of these results beyond a predominantly Caucasian, Italian population. The integration of innovative biomarkers, such as proteomic, metabolomic, and genetic profiles, could also help identify subgroups of athletes at particularly high risk of dyslipidemia and CV disease, paving the way for personalized prevention strategies.

9. Conclusions

Our study highlights that dyslipidemia is a relevant finding even among elite athletes, particularly in males and those practicing mixed sporting disciplines. Beyond its prevalence, dyslipidemia was associated with early signs of endothelial dysfunction, as evidenced by increased carotid intima-media thickness (IMT) despite preserved flow-mediated dilation (FMD). These results suggest that, even in highly trained individuals, lipid abnormalities may contribute to subclinical vascular remodeling without overt impairment of endothelial function.

Endurance athletes demonstrated the most favorable vascular and lipid profiles, supporting the notion that aerobic exercise exerts a protective effect on endothelial integrity and lipid metabolism, whereas athletes from mixed or skill-based sports exhibited higher dyslipidemia rates and thicker IMT values.

Overall, our findings underscore the need for periodic vascular assessment and lipid monitoring in elite athletes, since early endothelial alterations may represent the first step toward atherosclerotic changes despite high fitness levels. Future studies should further investigate the mechanisms linking dyslipidemia and endothelial remodeling in athletes, as well as the potential role of tailored nutritional or pharmacological interventions in preserving vascular health in this population.

10. Abbreviations

BAD: brachial artery diameter

BMI: body mass index

BSA: body surface area

CETP: cholesteryl ester transfer protein

CV: cardiovascular

EPC: endothelial progenitor cells

FMD: flow-mediated dilation

FT3: free triiodothyronine

FT4: free thyroxine

HDL: high-density lipoprotein

IMT: intima-media thickness

LDL: low-density lipoprotein

NO: nitric oxide

NSCI: non-spinal cord injury

PA: paralympic athletes

ROS: reactive oxygen species

SCI: spinal cord injury

TC: total cholesterol

TG: triglycerides

TSH: thyroid stimulating hormone

WC: waist circumference

11. References

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12. Tables

Table 1. Cholesterol Variation Across Athlete Subgroups (ref. 28,29,34,35,36,43,44,45).

Subgroup	LDL	HDL	TG	TC	Key notes and Clinical Implications
Male athletes	++	−	++	++	Higher LDL and TG; lower HDL compared to females; dyslipidemia prevalence ~35%
Female athletes	+	+++	−	+	Estrogen-related benefits; higher HDL and lower TC; dyslipidemia prevalence ~26%
Endurance sports	−−	+++	−−	=	Most favorable profile; dyslipidemia prevalence ~24%
Power sports	++	+	+	++	Elevated LDL & TG; prevalence ~38%
Skill sports	++	+	++	++	Lowest HDL and higher TG; dyslipidemia prevalence ~40%, especially in older males
Mixed sports	+	++	+	+	Intermediate values; dyslipidemia prevalence ~30%
Caucasians	++	+	++	++	Higher prevalence (~34%) of LDL ≥115 mg/dL or LDL/HDL ≥1.9
Afro-Caribbean	−	++	−	−	More favorable profile; lower LDL, LDL/HDL ratio, and non-HDL cholesterol
Paralympic (NSCI)	+	++	=	=	Higher HDL; Dyslipidemia prevalence ~35%; better lipid values in endurance sports
Paralympic (SCI)	++	+	=	+	Less favorable profile; influenced by reduced muscle mass, inflammation, and lower mobility.

Abbreviations: HDL: high-density lipoprotein; LDL: low-density lipoprotein; NSCI: non-spinal cord injury; SCI: spinal cord injury; TC: total cholesterol; TG: triglycerides. Symbols**:** +++ = very high/increased | ++ = high | + = slightly high | = = neutral | − = slightly low | −− = low | −−− = very low

Table 2. Comparison of main clinical, anthropometrics, blood tests and functional parameters between athletes with normal lipid profile and dyslipidemic population.

	Athletes, n=388			**Control group, n=100**			**Dyslipidemic**
	Normal Lipid Profile	**ALL dyslipidemic**	**p**	**Normal Lipid Profile**	**ALL dyslipidemic**	**p**	**Athletes vs. Sedentary**
N, (%)	292 (75.3)	96 (24.7)		63 (63)	37 (37)		
Age, years	29.3 ± 4.3	30.2 ± 5.5	0.126	30.5 ± 5.1	31.2 ± 6.5	0.528	0.329
Male, n (%)	**157 (53.8)**	**65 (67.7)**	**0.016**	**21 (33.3)**	**29 (78.4)**	**<0.0001**	0.228
Afro-Caribbean, n (%)	13 (4.4)	4 (4.2)	0.906	0 (0)	0 (0)	0.999	0.214
Smokers, n (%)	30 (10.3)	11 (11.4)	0.744	14 (22.2)	10 (27)	0.591	**0.027**
Familiarity for CVD, n (%)	79 (27)	25 (26)	0.846	22 (34.9)	14 (37.8)	0.772	0.183
Familiarity for dyslipidemia, n (%)	29 (9.9)	6 (6.3)	0.275	10 (15.9)	6 (16.2)	0.964	0.073
Height, m	**1.76 ± 0.10**	**1.79 ± 0.09**	**0.019**	**1.71 ± 0.07**	**1.77 ± 0.08**	**0.0001**	**0.383**
Weight, kg	**71.9 ± 13.1**	**77.3 ± 14.4**	**0.0007**	**67.7 ± 10.9**	**81.6 ± 9.7**	**<0.0001**	0.100
BMI, kg/m^2	**23 ± 2.6**	**24 ± 3**	**0.003**	**23.2 ± 2.8**	**25.9 ± 9.7**	**<0.0001**	**0.0007**

Overweight, n (%)	**53 (18.2)**	**29 (30.2)**	**0.012**	**19 (30.2)**	**20 (54.1)**	**0.017**	**0.010**
Fat mass, n (%)	14.6 ± 6.5	15.4 ± 6.7	0.652	-	-	-	-
WC, cm	**76.8 ± 7.5**	**80.2 ± 8.7**	**0.0003**	-	-	-	-
Fat, %	30.5 ± 4.4	30.8 ± 4.6	0.620	-	-	-	-
Protein, %	19.8 ± 4.3	20.7 ± 5.7	0.198	-	-	-	-
Carbs, %	49.6 ± 6.2	48.3 ± 8.3	0.162	-	-	-	-
Power, n (%)	80 (27.4)	24 (25)	0.646	-	-	-	-
Skills, n (%)	62 (21.2)	24 (25)	0.442	-	-	-	-
Endurance, n (%)	**92 (31.5)**	**18 (19)**	**0.016**	-	-	-	-
Mixed, n (%)	**59 (20.2)**	**30 (31.2)**	**0.025**	-	-	-	-
TC, mg/dL	**168.6 ± 22.6**	**205.7 ± 32.5**	**<0.0001**	**166 ± 21.6**	**203.9 ± 21.3**	**<0.0001**	0.748
LDL, mg/dL	**88 ± 16.7**	**126.9 ± 27.5**	**<0.0001**	**86.8 ± 12.9**	**134.4 ± 16.1**	**<0.0001**	0.119
HDL, mg/dL	**68.8 ± 15.1**	**60.9 ± 18.2**	**<0.0001**	**67.5 ± 13.4**	**58.5 ± 11**	**0.0009**	0.459
LDL/HDL	**1.34 ± 0.39**	**2.34 ± 1.53**	**<0.0001**	**1.3 ± 0.37**	**2.38 ± 0.54**	**<0.0001**	0.872
TG, mg/dL	**66.7 ± 22.2**	**96.6 ± 52.5**	**<0.0001**	**73.8 ± 21**	**92.1 ± 34.9**	**0.001**	0.631

AST, U/L	25 ± 9.8	26.1 ± 8.2	0.335	-	-	-	-
ALT, U/L	**20.9 ± 8.3**	**24.5 ± 10.7**	**0.0006**	-	-	-	-
IMT, mm	**0.57 ± 0.07**	**0.62 ± 0.05**	**<0.0001**	**0.56 ± 0.05**	**0.64 ± 0.05**	**<0.0001**	**0.005**
BAD, mm	352 ± 79.9	358.4 ± 76.5	0.492	**314.2 ± 75.9**	**362.1 ± 59.3**	**0.001**	0.795
FMD, %	13.8 ± 10.3	14.1 ± 11.7	0.839	**19.8 ± 10.7**	**12.4 ± 9.3**	**0.0008**	0.436
FMD < 7.1%	66 (22.6)	21 (21.9)	0.882	8 (12.7)	10 (27)	0.073	0.532
Rest HR, bpm	56.1 ± 9.9	55.9 ± 10.7	0.855	61.9 ± 7.6	62.7 ± 9.5	0.679	**0.001**
SBP, mmHg	115.2 ± 9.8	113.4 ± 10.3	0.143	117.3 ± 8.7	118.2 ± 9.2	0.654	0.354
DBP, mmHg	69.7 ± 7.3	69.6 ± 7.7	0.887	73.6 ± 6.9	73.2 ± 7.1	0.787	0.347

Abbreviations: AST: aspartate transaminase; ALT: alanine transaminase; BAD: brachial artery diameter; BMI: body mass index; BSA: body surface area; CVD: cardiovascular disease; DBP: diastolic blood pressure; FMD: flow-mediated dilation; HDL: high-density lipoprotein; HR: heart rate; IMT: intima-media thickness; LDL: low-density lipoprotein; SBP: systolic blood pressure; TC: total cholesterol; TG: triglycerides; WC: waist circumference.

Table 3. Gender differences in main clinical, lipidic profile and vascular morpho-functional parameters in athletes population.

N=388	Males	Females	p	Dyslipidemic Males	Normal lipid Males	p	Dyslipidemic Females	Normal lipid Females	p
N, (%)	222 (57.2)	166 (42.8)		65 (29.3)	157 (70.7)		31 (18.7)	135 (81.3)	
Age, years	29.8 ± 5.1	29.3 ± 5.2	0.296	30.7 ± 6	29.4 ± 4.6	0.087	29.1 ± 4	29.3 ± 4	0.886
BSA	**1.99 ± 0.20**	**1.74 ± 0.17**	**<0.0001**	**2.04 ± 0.20**	**1.97 ± 0.19**	**0.009**	1.76 ± 0.16	1.74 ± 0.16	0.472
Weight, kg	**79.6 ± 12.4**	**64.7 ± 10.3**	**<0.0001**	**83.1 ± 12.6**	**78.1 ± 12**	**0.005**	65.5 ± 9.8	64.5 ± 10.4	0.637
BMI, kg/m^2	**24 ± 2.6**	**22.2 ± 2.6**	**<0.0001**	**24.9 ± 2.7**	**23.6 ± 2.4**	**0.0008**	22 ± 2.6	22.2 ± 2.6	0.631
Overweight, n (%)	**62 (27.9)**	**20 (12)**	**0.0001**	**25 (38.5)**	**37 (23.6)**	**0.024**	4 (12.9)	16 (11.8)	0.930
Fat mass, n (%)	**11.1 ± 4.9**	**19.7 ± 5.2**	**<0.0001**	**12.8 ± 5.7**	**10.4 ± 4.3**	**0.045**	20.5 ± 5.6	19.5 ± 4	0.368
WC, cm	**82 ± 6.4**	**71.8 ± 5.8**	**<0.0001**	**84.4 ± 7**	**81.1 ± 5.8**	**0.0006**	72 ± 5.3	71.8 ± 5.9	0.885
Power, n (%)	59 (26.6)	45 (27.1)	0.907	17 (26.1)	42 (26.7)	0.927	7 (22.6)	38 (28.1)	0.461
Skills, n (%)	44 (19.8)	42 (25.3)	0.199	16 (24.6)	28 (17.8)	0.250	8 (25.8)	34 (25.2)	0.965
Endurance, n (%)	**72 (32.4)**	**38 (22.9)**	**0.039**	**11 (16.9)**	**61 (38.9)**	**0.001**	8 (25.8)	30 (22.2)	0.753
Mixed, n (%)	48 (21.6)	41 (24.7)	0.476	**21 (32.3)**	**27 (17.2)**	**0.012**	9 (29)	32 (23.7)	0.619

TC, mg/dL	176.3 ± 30.2	179.8 ± 29.6	0.252	**201.7 ± 31.9**	**165.8 ± 22.1**	**<0.0001**	**211.6 ± 34.3**	**172.2 ± 86.2**	**<0.0001**
LDL, mg/dL	**100.6 ± 27.1**	**93.7 ± 24**	**0.009**	**127.1 ± 27.8**	**89.6 ± 17.5**	**<0.0001**	**124.8 ± 27.7**	**86.2 ± 15.5**	**<0.0001**
HDL, mg/dL	**61.3 ± 15.3**	**74.2 ± 14.5**	**<0.0001**	**55.5 ± 15.9**	**63.7 ± 14.4**	**0.0003**	71.3 ± 17.8	74.9 ± 13.5	0.209
LDL/HDL	**1.8 ± 1.14**	**1.31 ± 0.44**	**<0.0001**	**2.58 ± 1.76**	**1.47 ± 0.41**	**<0.0001**	**1.83 ± 0.56**	**1.18 ± 0.29**	**<0.0001**
TG, mg/dL	**78.2 ± 39.8**	**68.6 ± 26.1**	**0.006**	**103.5 ± 57.8**	**67.7 ± 22**	**<0.0001**	**81.4 ± 34.8**	**65.4 ± 0.10**	**0.001**
IMT, mm	**0.59 ± 0.07**	**0.57 ± 0.06**	**0.004**	**0.62 ± 0.05**	**0.58 ± 0.06**	**<0.0001**	**0.60 ± 0.04**	**0.57 ± 0.06**	**0.016**
BAD, mm	**385.4 ± 72.9**	**311.1 ± 66**	**<0.0001**	386.4 ± 70.6	385 ± 73.9	0.902	305.6 ± 59.3	312.4 ± 67.4	0.598
FMD, %	**12.3 ± 10.1**	**16.1 ± 11**	**0.0006**	12.9 ± 10.8	12 ± 9.7	0.541	16.2 ± 12.9	16 ± 10.5	0.926
FMD < 7.1%	**58 (26.1)**	**29 (17.5)**	**0.043**	17 (26.1)	41 (26.1)	0.995	5 (16.1)	24 (17.8)	0.761

Abbreviations: BAD: brachial artery diameter; BMI: body mass index; BSA: body surface area; FMD: flow-mediated dilation; HDL: high-density lipoprotein; IMT: intima media thickness; LDL: low-density lipoprotein; TG: triglycerides; WC: waist circumference.

Table 4. Comparison of main clinical, anthropometrics, blood tests and vascular morpho-functional parameters according to different sporting category in athletes population.

N=388	**Skill**	**Power**	**Mixed**	**Endurance**	P pooled	P pairwise
N, (%)	86 (22.2)	104 (26.8)	89 (22.9)	110 (28.3)		
Age, years	31.6 ± 6.6	28.1 ± 2.3	29.9 ± 3.9	29 ± 4.5	<0.0001	**S vs. P, p<0.0001; S vs. M, p=0.048; S vs. E, p=0.001; P vs. M, p<0.0001;** P vs. E, p=0.078; M vs. E, p=0.112.
Male, n (%)	44 (51.2)	59 (56.7)	48 (53.9)	72 (65.5)	0.192	-
BMI, kg/m^2	23.5 ± 2.9	23.2 ± 2.8	23.5 ± 2.6	22.8 ± 2.6	0.276	-
Fat, %	32.2 ± 4.4	30.6 ± 4.5	30.7 ± 4.5	28.9 ± 3.9	0.0007	**S vs. P, p=0.039; S vs. E, p<0.0001; P vs. E, p=0.027; M vs. E, p=0.017;** S vs. M, p=0.053; P vs. M, p=0.875
Protein, %	20.1 ± 5.2	20 ± 4.5	20.3 ± 3.9	19.7 ± 5.4	0.921	-

Carbs, %	47.7 ± 7.4	49.2 ± 6.9	48.9 ± 6.2	51.4 ± 6.2	0.019	**S vs. E, p=0.002; M vs. E, p=0.020;** P vs. M, p=0.784; S vs. M, p=0.308; P vs. E, p=0.056; S vs. P, p=0.227.
Dyslipidemia	23 (26.7)	19 (18.2)	21 (23.6)	16 (14.5)	0.150	-
TC, mg/dL	185 ± 29.7	176 ± 31.8	176.9 ± 28.2	174.5 ± 28.8	0.078	-
LDL, mg/dL	103 ± 25.5	97.2 ± 27	99.5 ± 26	92.1 ± 24.4	0.028	**S vs. E, p=0.002; M vs. E, p=0.043;** S vs. P, p=0.135; S vs. M, p=0.370; P vs. M, p=0.555; P vs. E, p=0.153.
HDL, mg/dL	67.8 ± 14.9	65.5 ± 16.2	62.4 ± 15.9	70.7 ± 16.6	0.003	**S vs. M, p=0.022; P vs. E, p=0.023 M vs. E, p=0.005;** S vs. P, p=0.316; S vs. E, p=0.216; P vs. M, p=0.186.
LDL/HDL	1.61 ± 0.6	1.57 ± 0.6	1.85 ± 1.6	1.38 ± 0.50	0.005	**S vs. E, p=0.004; P vs. E, p=0.012; M vs. E, p=0.004;** P vs. M, p=0.097; S vs. P, p=0.576; S vs. M, p=0.210.
TG, mg/dL	77.2 ± 30.6	72.5 ± 28.4	86.7 ± 51.4	62.9 ± 20.2	<0.0001	**S vs. E, p=0.0001; P vs. M, p=0.017; P vs. E, p=0.004; M vs. E, p<0.0001;** S vs. P, p=0.275;

						S vs. M, p=0.146.
IMT, mm	0.58 ± 0.07	0.57 ± 0.06	0.58 ± 0.06	0.59 ± 0.06	0.154	-
BAD, mm	338.4 ± 73.7	342.1 ± 78.4	346.2 ± 64.5	382.7 ± 86.4	<0.0001	**S vs. E, p=0.0002; P vs. E, p=0.0004; M vs. E, p=0.001;** S vs. P, p=0.743; S vs. M, p=0.459; P vs. M, p=0.694.
FMD, %	16.3 ± 10.4	16.2 ± 11.2	13 ± 9.8	10.6 ± 9.9	0.0001	**S vs. M, p=0.030; S vs. E, p=0.0001; P vs. M, p=0.039; P vs. E, p=0.0002;** M vs. E, p=0.087; S vs. P, p=0.908.
FMD < 7.1%	16 (18.6)	19 (18.3)	16 (18)	36 (32.7)	0.023	**S vs. E, p=0.026; P vs. E, p=0.015; M vs. E, p=0.018;** S vs. P, p=0.953; S vs. M, p=0.915; P vs. M, p=0.958.
Rest HR, bpm	58.8 ± 9.5	56.8 ± 10.2	55.5 ± 10	53.5 ± 9.8	0.003	**S vs. M, p=0.031; S vs. E, p=0.0003; P vs. E, p=0.020;** S vs. P, p=0.173; P vs. M, p=0.397; M vs. E, p=0.171.
SBP, mmHg	113.3 ± 10.1	114.8 ± 10.2	116.1 ± 8.7	114.9 ± 10.5	0.335	-

DBP, mmHg	69.5 ± 7.3	69.6 ± 7.6	70.1 ± 7	69.6 ± 7.7	0.974	-

Abbreviations: BAD: brachial artery diameter; BMI: body mass index; BSA: body surface area; DBP: diastolic blood pressure; E: endurance; FMD: flow-mediated dilation; HDL: high-density lipoprotein; IMT: intima-media thickness; LDL: low-density lipoprotein; M: mixed; P: power; S: skill; SBP: systolic blood pressure; TC: total cholesterol; TG: triglycerides;.

Table 5. Comparison between study results and literature findings on dyslipidemia, vascular function, and sport-specific effects

Aspect	Findings in our study	General Findings in literature
Prevalence of dyslipidemia	24.7% of elite athletes; mainly ↑LDL-C, less hypo-HDL and hyper-TG	Dyslipidemia common in general population; prevalence reduced by aerobic exercise, but not abolished (ref 28)
LDL cholesterol	Elevated in ~20% of athletes, especially males	Exercise reduces LDL-C, but effects less pronounced than on HDL-C (ref.29)
HDL cholesterol	Generally higher in athletes, but hypo-HDL more common in females	Aerobic exercise consistently increases HDL-C (ref 29,44,57-60)
Triglycerides	Low prevalence of hypertriglyceridemia in athletes	Exercise decreases triglycerides via ↑lipoprotein lipase activity (ref 33)
Gender differences (lipids)	Males: ↑LDL-C, ↓HDL-C, ↑TG vs. females	Premenopausal women: estrogen-mediated protective lipid profile (ref 34)
Gender differences (vascular)	Males: ↑IMT, ↓FMD vs. females	Men generally show thicker IMT and lower FMD (ref 34)
Endurance athletes	Best lipid profile: lowest LDL, highest HDL, lowest TG	Aerobic training strongly improves lipid metabolism and vascular health (ref 35,43)
Power/Skill/Mixed sports	Skill: worst lipid profile; Mixed: highest dyslipidemia prevalence	Lower aerobic load → less favorable lipid effects (ref 44)
Dietary habits	Endurance: lowest fat, highest carbohydrate intake; Skill: higher fat intake	Nutrition interacts with exercise in shaping lipid profile (ref 43,44)
Carotid IMT	↑IMT in dyslipidemic athletes; some with focal thickening	↑IMT = early atherosclerosis marker; observed also in athletes (ref 25)
FMD (athletes with dyslipidemia)	Preserved FMD despite ↑IMT	Exercise preserves endothelial function despite risk factors (ref 60-62
FMD (endurance athletes)	Lower FMD despite favorable lipid profile	Larger artery diameters reduce relative FMD response (ref 60)
Comparison with sedentary controls	Athletes: less dyslipidemia, preserved FMD, but ↑IMT in dyslipidemic subgroup	Sedentary dyslipidemic: both ↑IMT and ↓FMD (ref 43,44,45)

13. Figure Legends

Figure 1. Brachial vascular ultrasound echography. Panel A. Measurement of rest brachial artery diameter. Panel B. Assessment of brachial artery diameter after deflating arm cuff.

Figure 2. Carotid vessel ultrasound echography. Automatic detection and calculation of intima media thickness.

Figure 3. Graphical representation of dyslipidemic athletes and their distribution according to the type of altered lipidic value. *Abbreviations*: HDL: high-density lipoprotein; LDL: low-density lipoprotein; TG: triglycerides.

Figure 4. Carotid vessel ultrasound echography. Focal fibrous thickening of carotid vessels found in athletes (Panel A and B) and sedentary subjects (Panel C and D).

Figure 5. Simple linear regression analysis between IMT and lipidic components in athletes. Panel A: LDL; Panel B: HDL; Panel C: LDL/HDL ratio; Panel D: TG. *Abbreviations*: HDL: high-density lipoprotein; LDL: low-density lipoprotein; TG: triglycerides.

Figure 6. Simple linear regression analysis between IMT and LDL in athletes population. Panel A: dyslipidemic athletes; Panel B: athletes with normal lipid profile. *Abbreviations*: HDL: high-density lipoprotein; LDL: low-density lipoprotein; TG: triglycerides.

14. Figures

Figure 1

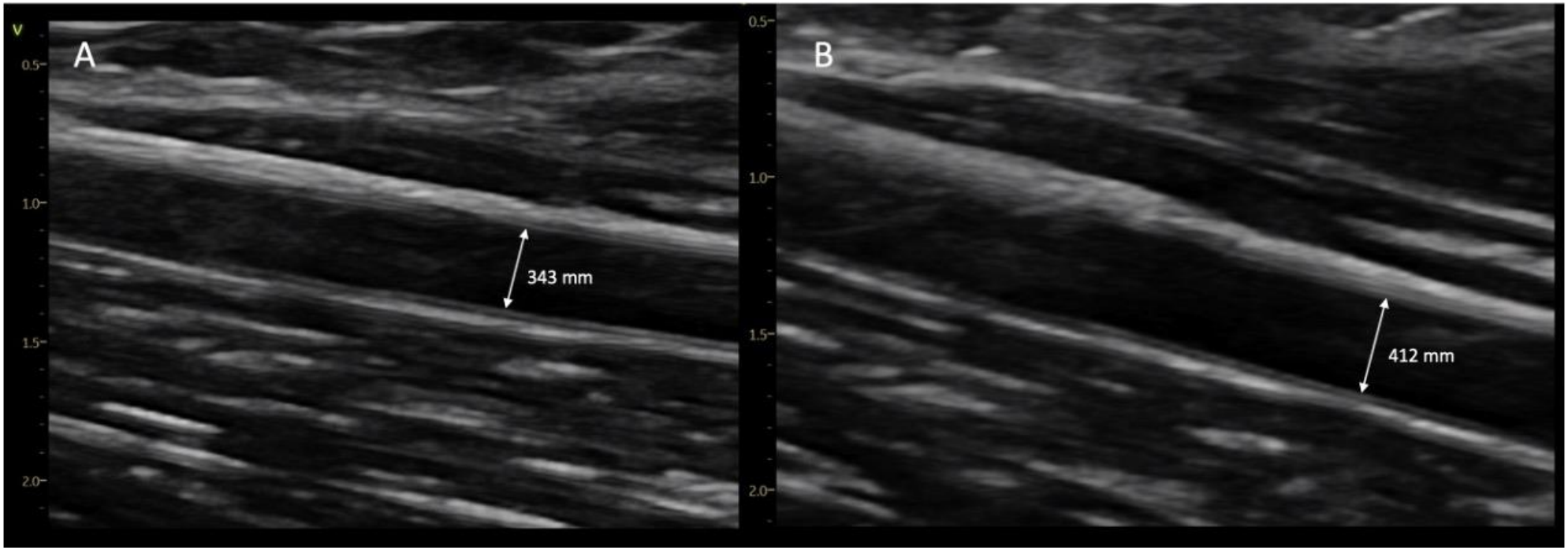


Figure 2.

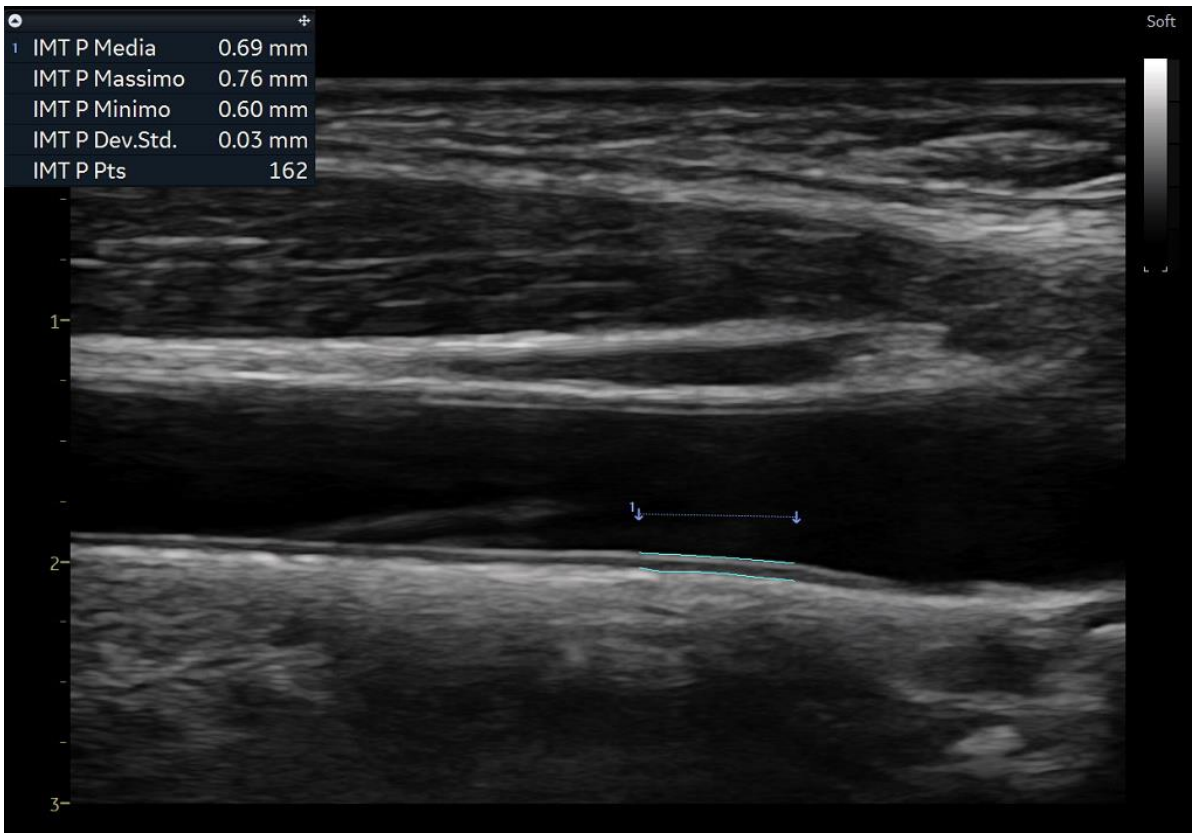

IMT P Media 0.69 mm
IMT P Massimo 0.76 mm
IMT P Minimo 0.60 mm
IMT P Dev.Std. 0.03 mm
IMT P Pts 162
Soft
1
2
3

Figure 3.

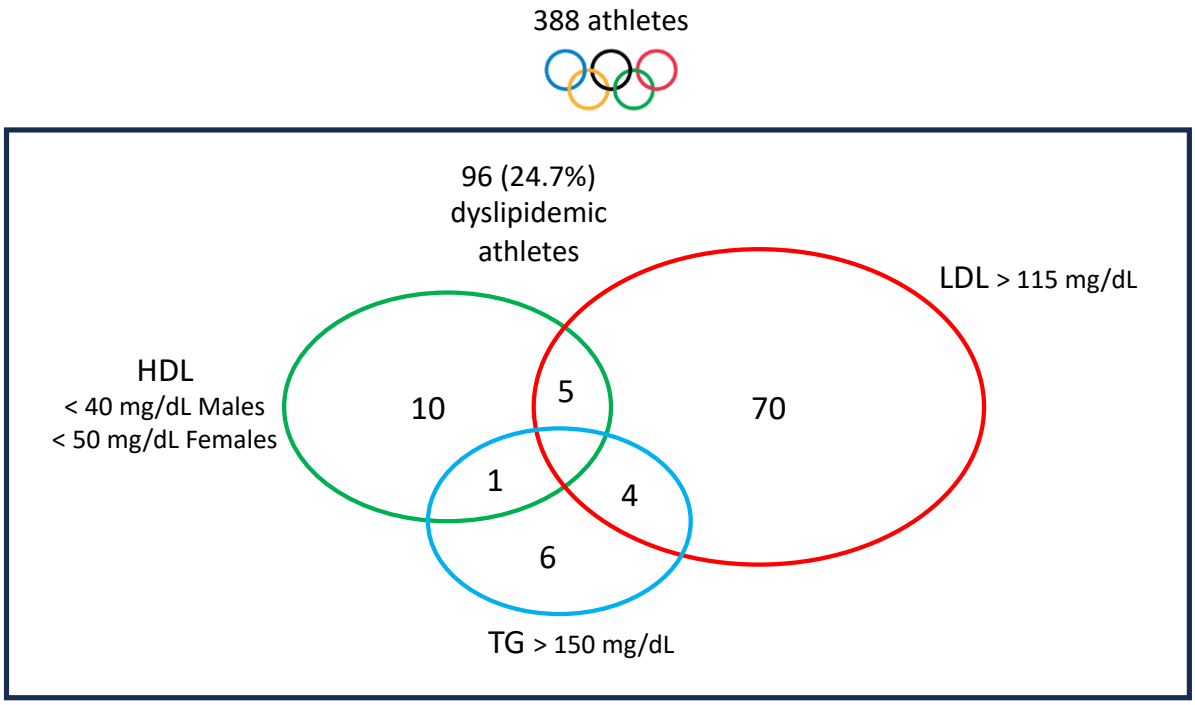

388 athletes
96 (24.7%)
dyslipidemic
athletes
LDL > 115 mg/dL
HDL
< 40 mg/dL Males
< 50 mg/dL Females
10
5
70
1
4
6
TG > 150 mg/dL

Figure 4.

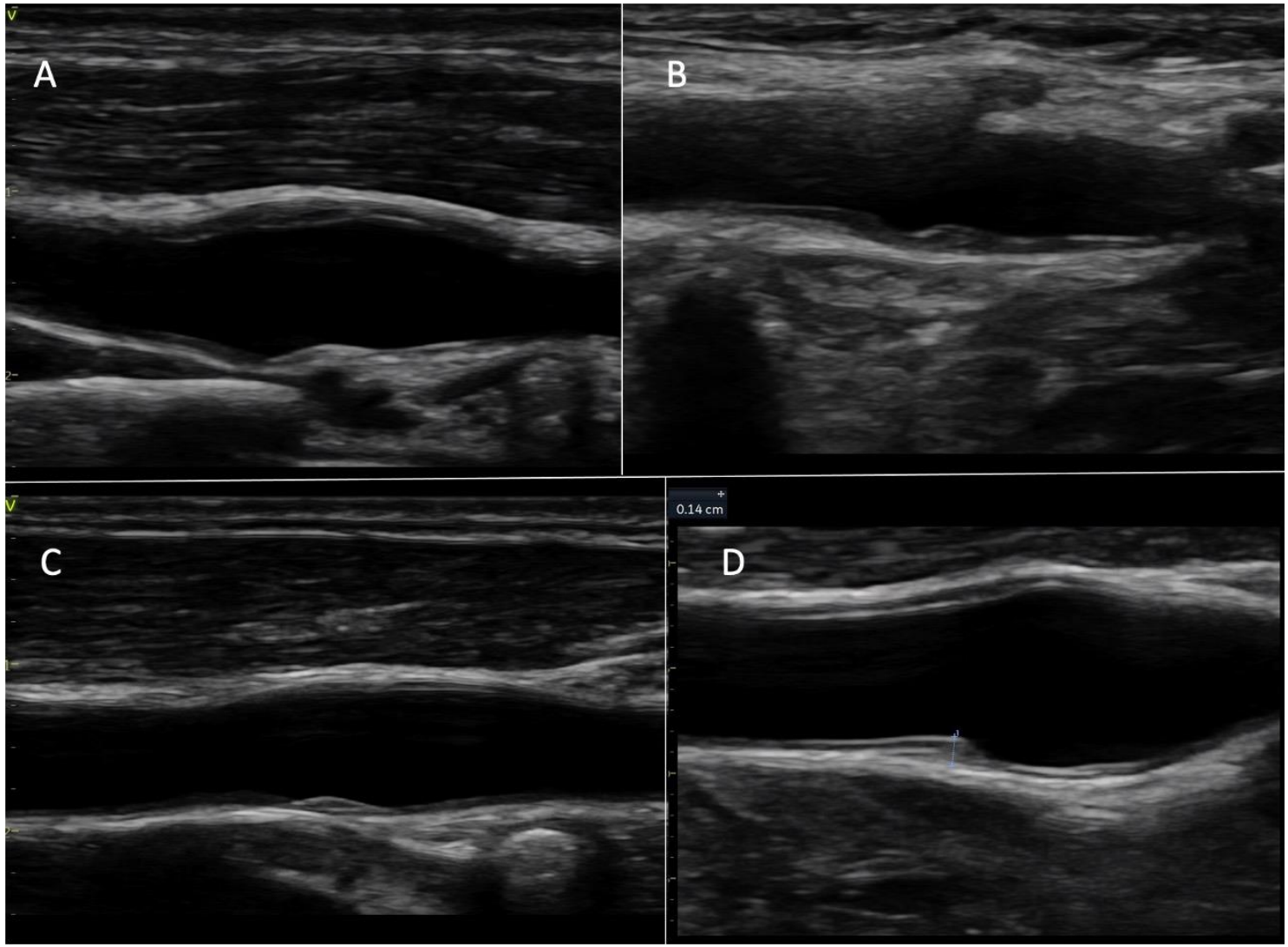


Figure 5.

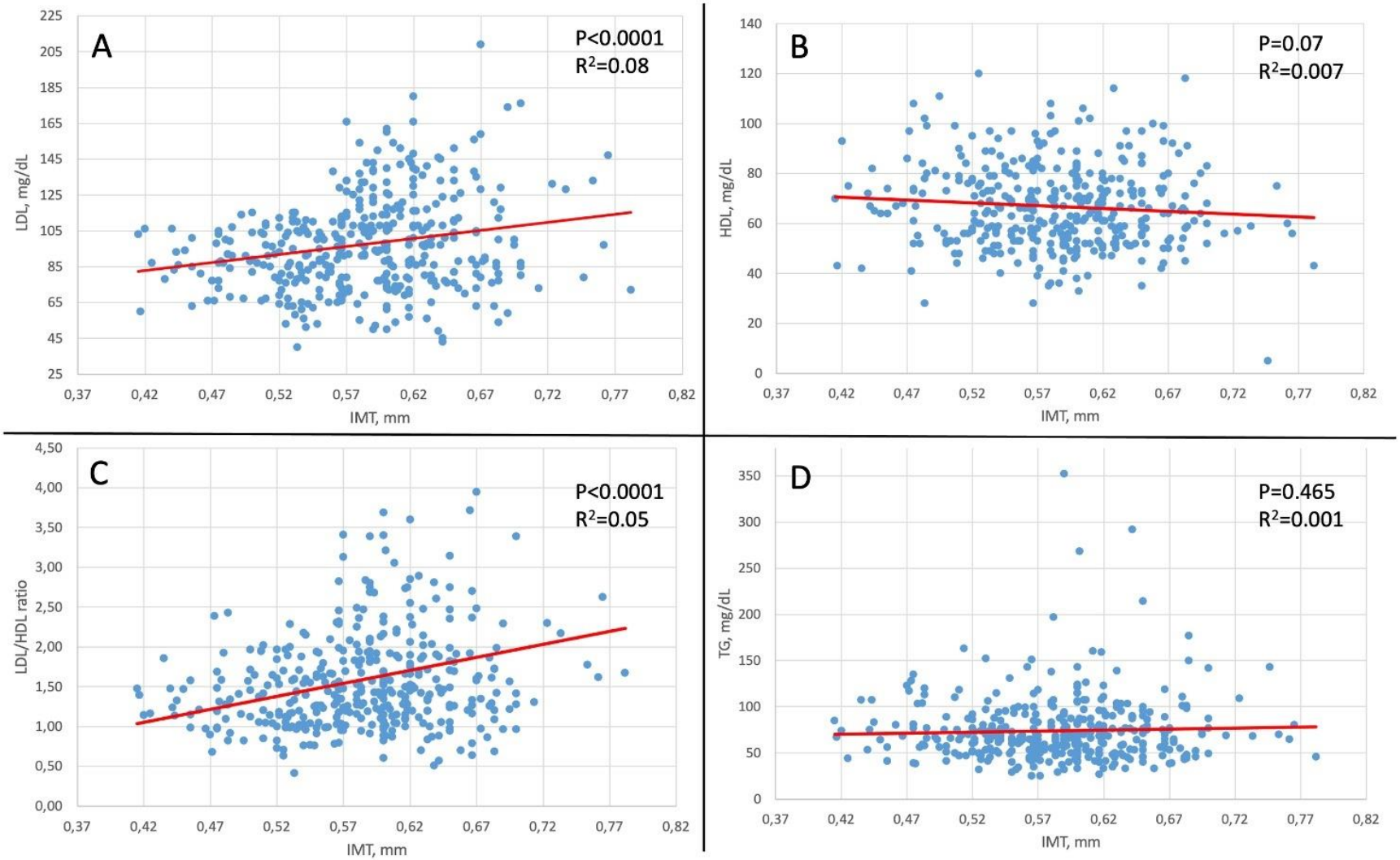
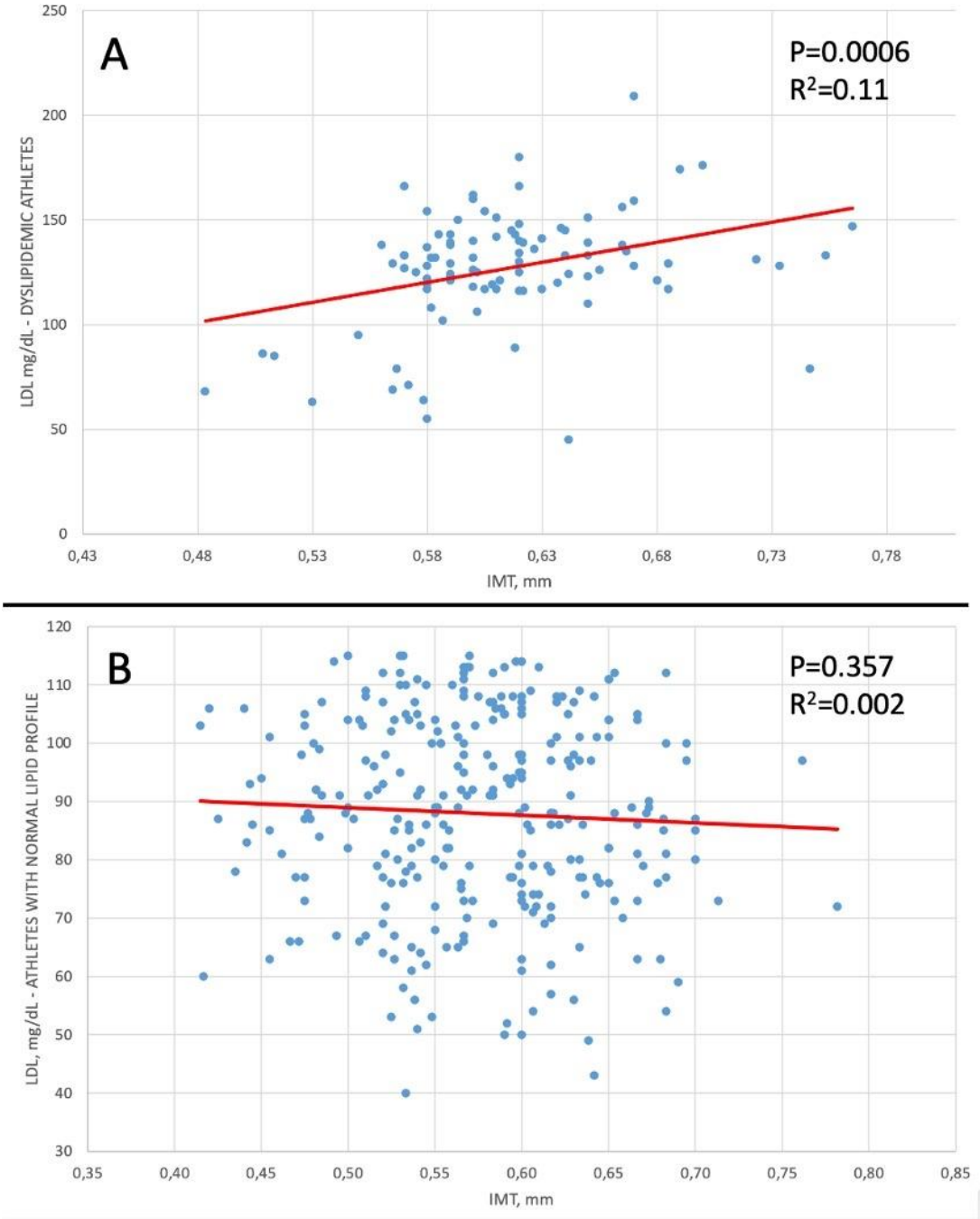

A
P<0.0001
R²=0.08
LDL, mg/dL
IMT, mm
B
P=0.07
R²=0.007
HDL, mg/dL
IMT, mm
C
P<0.0001
R²=0.05
LDL/HDL ratio
IMT, mm
D
P=0.465
R²=0.001
TG, mg/dL
IMT, mm

Figure 6.


A
P=0.0006
R²=0.11
LDL mg/dL - DYSLIPIDEMIC ATHLETES
IMT, mm
B
P=0.357
R²=0.002
LDL, mg/dL - ATHLETES WITH NORMAL LIPID PROFILE
IMT, mm

15. Scientific papers published related to PhD thesis

1. **G. Di Gioia,** F. Vespasiano, A. Ferrera, A. Segreti, E. Lemme, M.R. Squeo, Athlete's artery: Brachial vascular remodeling in elite athletes practicing different sporting disciplines, **Science & Sports**, 2025, ,ISSN 0765-1597, https://doi.org/10.1016/j.scispo.2024.12.006.
2. **Di Gioia, G**., Buzzelli, L., Ferrera, A. Maestrini, V., Squeo, MR., Lemme, E., Monosilio, S. Serdoz, A., Pelliccia A. Influence of Persistently Elevated LDL Values on Carotid Intima Media Thickness in Elite Athletes. **High Blood Press Cardiovasc Prev** (2025). https://doi.org/10.1007/s40292-024-00698-2
3. **Di Gioia, G.**; Ferrera, A.; Celeski, M.; Mistrulli, R.; Lemme, E.; Mango, F.; Squeo, M.R.; Pelliccia, A. Lipid Accumulation Product and Cardiometabolic Index as Effective Tools for the Identification of Athletes at Risk for Metabolic Syndrome. **Life** 2024, 14, 1452. https://doi.org/10.3390/life14111452
4. **Di Gioia G**, Buzzelli L, Maestrini V, Squeo MR, Lemme E, Monosilio S, Serdoz A, Fiore R, Zampaglione D, Segreti A, Pelliccia A. Long-Term Evaluation of Lipid Profile Changes in Olympic Athletes. **Int J Sport Nutr Exerc Metab**. 2024 Jun 25:1-8. doi: 10.1123/ijsnem.2023-0266. Epub ahead of print. PMID: 38917988.
5. **G Di Gioia**, V Maestrini, S Monosilio, E Lemme, M R Squeo, A Serdoz, D Zampaglione, R Fiore, G Paoletti, A Pelliccia, Effects of dyslipidemia on endothelial morpho-functional parameters in a cohort of elite athletes practicing different sporting disciplines, **European Journal of Preventive Cardiology**, Volume 31, Issue Supplement_1, June 2024, zwae175.358, https://doi.org/10.1093/eurjpc/zwae175.358
6. **G Di Gioia**, M R Squeo, E Lemme, G Paoletti, V Maestrini, S Monosilio, A Serdoz, R Fiore, D Zampaglione, A Pelliccia, Athlete's artery: brachial vascular remodeling in elite athletes practicing different sporting disciplines, **European Journal of**

Preventive Cardiology, Volume 31, Issue Supplement_1, June 2024, zwae175.278, https://doi.org/10.1093/eurjpc/zwae175.278

7. **Di Gioia, G.**, Buzzelli, L., Ferrera, A., Squeo, MR., Lemme, E., Pelliccia, A. Differences Between Afro-Caribbean and White Caucasian Olympic Athletes in Plasma Lipids Profile: A Cross-Sectional Single Center Study. **High Blood Press Cardiovasc Prev** (2024). https://doi.org/10.1007/s40292-024-00654-0
8. **Di Gioia, G**., Vespasiano, F., Mango, F., Maestrini, V., Monosilio, S., Squeo, MR., Lemme, E., Bernardi, M., Pelliccia, A. Cardiovascular Risk Profile in Master Paralympic Athletes, a High-Risk Undertreated Population: A Cross-Sectional Longitudinal Study. **High Blood Press Cardiovasc Prev** (2024). https://doi.org/10.1007/s40292-024-00648-y
9. **Di Gioia, G.**; Crispino, S.P.; Maestrini, V.; Monosilio, S.; Squeo, M.R.; Lemme, E.; Segreti, A.; Serdoz, A.; Fiore, R.; Zampaglione, D.; Pelliccia A. Prevalence of Hyperuricemia and Associated Cardiovascular Risk Factors in Elite Athletes Practicing Different Sporting Disciplines: A Cross-Sectional Study. **J. Clin. Med**. 2024,13,560. https://doi.org/ 10.3390/jcm13020560
10. **Di Gioia G**, Buzzelli L, Maestrini V, Nenna A, Monosilio S, Squeo MR, Lemme E, Pelliccia A. Lipid Profile in Olympic Athletes Proposal for a "Lipid Athlete Score" as a Clinical Tool to Identify High-Risk Athletes. **J. Clin. Med**. 2023, 12, 7449. https://doi.org/ 10.3390/jcm12237449
11. **Di Gioia G**, Coletti F, Buzzelli L, Maestrini V, Monosilio S, Segreti A, Squeo MR, Lemme E, Nenna A, Pelliccia A. Influence of the Type of Disability and Sporting Discipline on Lipid Profile in a Cohort of Italian Paralympic Athletes. **Am J Cardiol** 2024;210:107−112
12. Buzzelli L, Segreti A, Di Gioia D, Lemme E, Squeo MR, Nenna A, **Di Gioia G**. Alternative lipid lowering strategies: State-of-the-art review of red yeast rice.

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