Original Research Article

Jörn Rittweger*, Wolfram Sies, Miriam Capri and Dominik Pesta

Physical activity and cardiometabolic risk factors in sprint and jump-trained masters athletes, young athletes and non-physically active men

https://doi.org/10.1515/teb-2024-0021
Received July 9, 2024; accepted October 10, 2024;
published online December 9, 2024

Abstract

Objectives: Assessing physical activity and cardiometabolic risk in masters athletes as an example of very high physical activity at old age.
Methods: Forty-three men were studied in full factorial design, either as sprint or jump-trained masters athletes (MA, n=10, age 60–75 years), as young sprint or jump-trained athletes (YA, n=10, age 20–35 years), older control participants (OC, n=11, age 60–75 years) or as young control participants (AC, n=12, age 20–35 years). We performed bioelectrical impedance analysis and assessed serum markers of lipids and glucose metabolism and C-reactive protein, structured training hours, and habitual activity via mobile actimetry.
Results: Body fat was greater in OC than in MA (23.9 [SD 4.2] % vs. 14.0 [SD 5.7] %, p<0.001), and also greater than in YA and YC (both p<0.001). Weekly training hours were comparable between MA and YA (7.9 [SD3.3] hours vs. 11.1 [SD 4.8] hours, p=0.69). Habitual walking distance was greater in MA than in OC (7,387 [SD 4,923] m/day vs. 4,110 [SD 1,772] m/day, p=0.039), and so was habitual running distance (667 [SD690] m/day vs. 132 [427] m/day, p<0.001). HOMA-index was greater in OC than in MA (2.07 [SD 1.39] vs. 0.80 [SD 0.41], p=0.0039), and so was C-reactive protein (1.35 [SD 1.74] mg/l vs. 0.58 [SD 0.27] mg/ml, p=0.018), whereas serum lipids showed only moderate or no effect (all p between 0.036 and 0.07).
Conclusions: Improved body composition and physical activity levels in MA are associated with lower cardiometabolic risk, which seems more pronounced for insulin sensitivity and inflammaging than for lipid metabolism.

Keywords: inflammaging; cardiovascular health; exercise training; track and field athletics; aging

Introduction

Physical activity is, in combination with diet, the most important modifiable determinant of health and well-being, in particular with regards to the risks of cardiovascular disease [1]. Physical activity at old age reduces all-cause mortality and cause-specific mortality for cardiovascular diseases, cancer, respiratory diseases, diabetes and others [2, 3]. Various routes convey these health-promoting effects across the lifespan. Firstly, cardiovascular function is improved, which includes enhanced stroke volume, ejection fraction and cardiac output [4], and reductions in blood pressure and arterial stiffness [5]. Second, the metabolic route encompasses improvement of blood lipid profiles [6] and maintenance of insulin sensitivity [7]. Exercise stimulates release of myokines [8], *i.e.* signaling molecules from skeletal muscle, which are related to not only metabolism and energy shuttling, but also more wide-spread effects. This may explain positive exercise effects on mental health [9] and cognitive functioning [10]. Finally, exercise has also been shown to moderate age-related low-grade inflammation [11], which is also known as 'inflammaging' [12], and which may contribute to the onset of age-related diseases [13]. For all these reasons, the World Health Organization recommends a minimum of 150 min of moderate or 75 min of vigorous physical activity per week and regular muscle-strengthening exercises [14] – a recommendation that is

***Corresponding author: Jörn Rittweger**, Institute of Aerospace Medicine, German Aerospace Center, 51147 Cologne, Germany; and Department of Pediatrics and Adolescent Medicine, University Hospital Cologne, Germany, E-mail: Joern.Rittweger@dlr.de
Wolfram Sies, Institute of Aerospace Medicine, German Aerospace Center, Cologne, Cologne, Germany
Miriam Capri, DIMEC – Department of Medical and Surgical Sciences, Alma Mater Studiorum, University of Bologna, Bologna, Italy; and Alma Mater Research Institute on Global Challenges and Climate Change, University of Bologna, Bologna, Emilia-Romagna, Italy
Dominik Pesta, Institute of Aerospace Medicine, German Aerospace Center, Cologne, Cologne, Germany; Center for Endocrinology, Diabetes and Preventive Medicine (CEDP), University Hospital Cologne, Cologne, Germany; and Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), University of Cologne, Cologne, Germany. https://orcid.org/0000-0002-5089-3586

under-achieved in large fractions of the population, in particular in older people [15].

Masters athletes (MA) "are typically older than 35 years of age and systematically train for, and compete in, organized forms of sport specifically designed for older adults" [16], typically organized in 5-year age bands. In that respect, MA constitute an example of aging that differs from the general population [17–19]. MA are amateurs, and the leading motivation drivers for them are competition, followed by well-being (*i.e.* satisfaction with one's life in a broader sense) and health (*i.e.* absence of disease) [20]. Given that the competitive element is typically much less pronounced in recreationally physically active people, MA offer a unique opportunity for studying the interplay of aging, exercise and health. As much as they are driven by ambition, they will optimize their training volume, intensity and structure in order to maximize their athletic performance, and thus challenging themselves more vigorously than most other people of their age would.

While MA are often depicted as healthier than non-exercising older individuals, there is currently insufficient evidence to support this claim. A retrospective study found a reduction in mortality rate in former elite athletes as compared to their siblings and concluded that this could be explained by genetic differences, adaptation to aerobic training and healthy life style [21], even though life style had not been assessed in that study. Therefore, we here report a secondary data analysis of the masters athletic laboratory study of intramuscular connective tissue (MALICoT) [22] with the primary aim of comparing cardiometabolic health between MA and young (20–35 years) and older (60–75) control participants.

MA do not only engage in structured training with an intent to increase fitness, but also in habitual physical activity outside their structured training units. Since both must be assumed to improve health, and since very little is known about physical activity outside structured training units in MA, we sought to independently assess both types of activity as a secondary aim. The summary of this study is presented in Figure 1.

Materials and methods

Study design and conduct

The MALICoT study was set up as a cross-sectional study in full factorial design with four groups, namely young control (YC), young athletes (YA), masters athletes (MA) and old control (OC) participants. The study was conducted from September 2020 until May 2021 in the envihab laboratory of the Institute of Aerospace Medicine at the German Aerospace Center (DLR) in Cologne, Germany. The primary aim of the MALICOT study was assessment of intramuscular connective tissue (primary endpoint: endomysium thickness). Following the rationale that intramuscular connective tissue has a mechanical role in the provision of elastic stiffness, we chose to focus on the calf musculature of sprinters and jumpers, since stiffness is of utmost importance for this athletic group [23]. A sample size estimation for that endpoint yielded n=12 per group, and thus 48 participants in total (for details see [22]). Given that there are much fewer female than male MA (Rittweger et al., in preparation), that the study encompassed muscle biopsy sampling, and based on our experience that women are more difficult to recruit for biopsy studies than men, inclusion of women into the study seemed impossible we therefore focused on male participants only. Here we report a secondary, exploratory data analysis of cardiometabolic risk factors of MALICoT – the primary outcome of MALICoT has yet to be published.

The study was ethically reviewed and approved by the Medical Council Northrhine-Westfalia (Landesärztekammer Nordrhein) with identifier 2018296. It was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and it was registered at the German clinical trials register (www.drks.de, registration no. DRKS00015764) before study commencement.

Participants

Participants were recruited from an existing participant data base at DLR, through contacts with athletes, via posters at the German Sports University Cologne and via social media. Inclusion criterion was age between 20 and 35 years for the young groups (YA, YC), and age between 60 and 75 for the old groups. However, one participant was enlisted at age 59, and he was included in the spring 2021 prior to study closure, i.e. a few weeks before completing 60 years of age. Participants for the athletic groups (YA, MA) were included only if they trained for jumping or sprint running and if they competed at national or international level in these disciplines. All athletic participants were amateurs. Participants for the non-physically active groups were included only if they did not follow any structured training, and if their habitual physical activity was ≤25 metabolic equivalents for task (METs) per week, as assessed by the Freiburg questionnaire [24]. Exclusion criteria for all groups were smoking, diabetes mellitus (estimated based on available fasted serum glucose levels), a history of cardiovascular disease or any other condition that could have impact on the musculoskeletal system. All participants gave their written

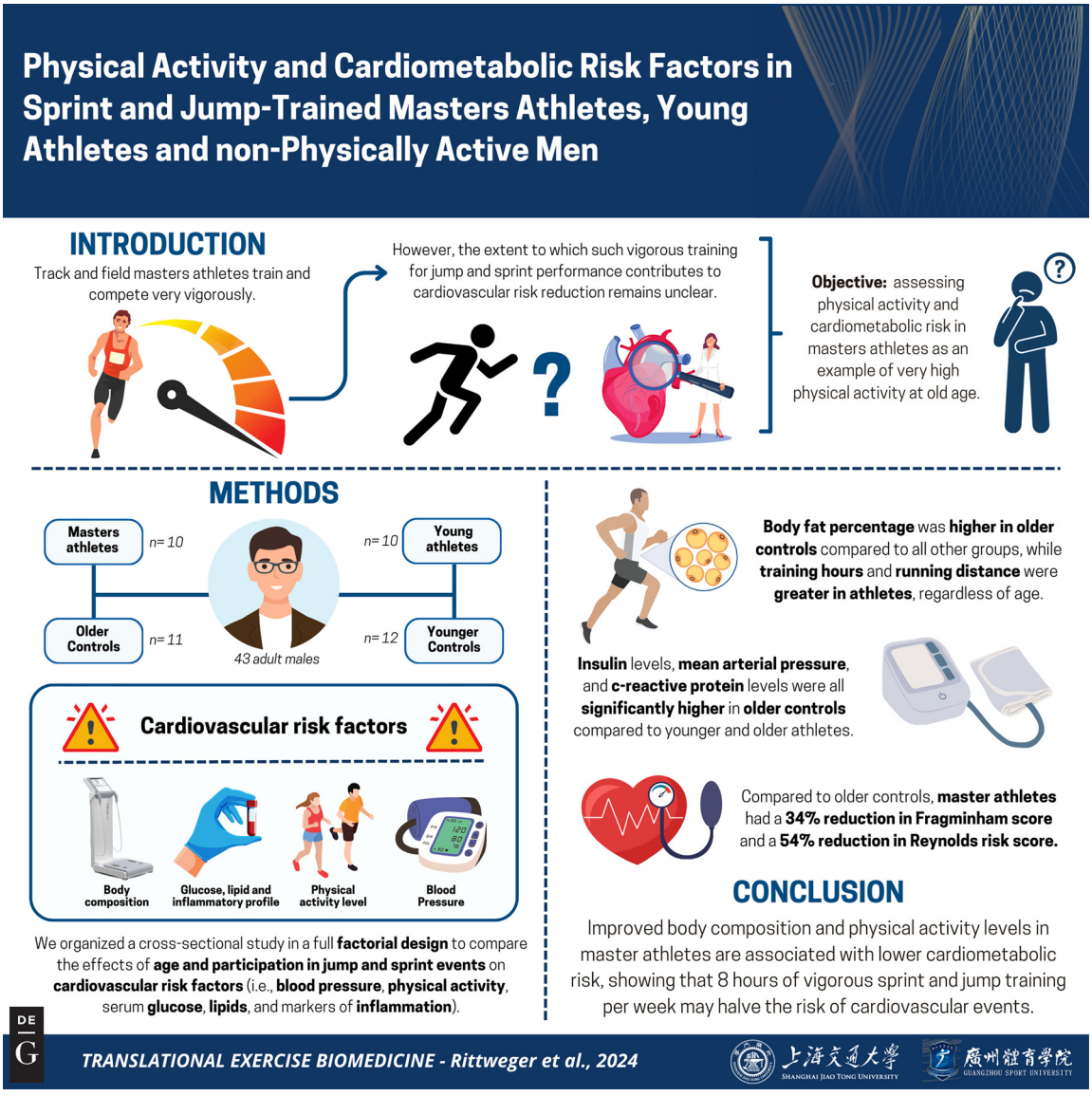

Figure 1: Graphical representation of this study. Key points: (1) Masters athletes (MA) have lower body fat and higher physical activity levels than non-physically active older men. (2) MA show better insulin sensitivity and lower inflammaging markers compared to older controls. (3) The study suggests MA have reduced cardiometabolic risk, particularly for insulin sensitivity. Figure created with BioRender.

informed consent prior to being included in the study. More information about the study setting is contained in our previous publications [25, 26].

Assessments

During the inclusion visit, blood pressure was measured after a 10-min rest in seated position with a manual sphygmomanometer (Boso, Germany). Two measurements were taken within a 2-min interval and the average was noted. At the end of the inclusion visit, the actibelt was demonstrated to the participant. The actibelt (Trium, Germany) is a triaxial accelerometer that allows continuous high-fidelity recordings for a period >2weeks. More specifically, the RCT2 model was used in this study. Whilst the actibelt can capture running and walking behavior, it is not geared to assess training elements like stretching, resistance training or plyometric exercises. Hence, we chose to exclude training periods, so that the actibelt data collection aimed at understanding whether the athletic groups' physical activity levels differ from the control groups' physical activity levels by the structured training only, or also by habitual physical activity outside their structured training units. Accordingly, participants were instructed to wear the actibelt for 7 successive days, taking it off only at night, when showering and during

structured training. If the testing visit was scheduled within the subsequent 1–2 weeks, then the actibelt was handed out during the inclusion visit, otherwise it was sent via mail. The hours of structured training were assessed via the question 'how many hours do you train in a typical week?' [27].

For the testing visit, participants arrived in the morning of a separate day after an overnight fast. A blood sample was taken from an antecubital vein. Serum was automatically assayed for concentrations of HbA1c with an HLC-723 G11 HPLC analyzer (Tosoh) for glucose, triglycerides, cholesterol, HDL-cholesterol (HDL) and C-reactive protein (CRP) with an Atellica CH (Siemens), and for Insulin with an Atellica IM (Siemens). Next, body height and mass were assessed on a stadiometer, and body composition was assessed via bioelectrical impedance analysis (BIA) with an InBody 720 (InBody, South Korea).

Data processing

Manually acquired data (blood pressure, body height, body mass, training hours) were administered with a dedicated Redcap database. These data, the data exported from the InBody software and data from the biochemical analysers were merged and further processed with R (www.r-project.org) and the RStudio environment. Body mass index (BMI) was computed as the body's mass/height^2. Blood pressure amplitude (BPamp) was computed from systolic and diastolic blood pressures (BPsys and BPdia, respectively) as BPsys-BPdia, and mean arterial pressure (MAP) was computed as (2 BPdia + BPsys)/3. Appendicular skeletal muscle mass (ASMM) was computed from the BIA data following Sergi's equation [28], and the ASMM-index was computed analogous to BMI as ASMM/mass^2. Actibelt data were captured at 100 Hz with a range between −6 g to +6 g. They were processed with the Stepwave algorithm [29]. This algorithm first performs step detection algorithm that detects local extremes (= heel strikes) via adaptive thresholds and sliding windowing. Next, gait speed is assessed via a support vector regression machine. The actibelt software then computes activity parameters such as average daily walking speed, wearing time and daily number of walking steps. Where actibelt recordings were <10 h per day, the data for that day and participant were excluded from further analyses. Where CRP readings were below the limit of biochemical detection (=0.5 mg/L), these missing values were set to the limit of detection. Further, the 10-year risk to develop coronary heart disease (CHD.risk.Framingham) was computed from age, cholesterol, HDL, BPsys, BPdia and smoking and diabetes status (both negative in this study), using a custom-made R-implementation of the scoring tables of Wilson et al. [30]. As that algorithm only applies to age ≥30, ages <30 were set to 30 for this computation. This may have a small effect for age comparisons, but will not lead to any bias with regards to statistical effects of athletic participation. Finally, we also computed the Reynolds cardiovascular disease risk score (CVD.risk.Reynolds) [31, 32], which includes CRP in addition to the variables covered by CHD risk. Framingham. Homeostatic Model Assessment of insulin resistance (HOMA-IR) was calculated according to the formula: fasting insulin (microU/L) x fasting glucose (nmol/L)/22.5.

Statistical analyses

All statistical analyses were carried out with R. Throughout the participant recruitment phase, biometric data (age, body height and body mass) of participants were continuously assessed, one-way analysis of variance (ANOVA) was used to statistically safeguard comparability of groups.

For evaluation of the study outcome, group comparisons were performed by ANOVA (R function 'lm'), and model criticism was effectuated by residual plots and quantile-quantile plots. Data were boxcox-transformed where required (R function 'MASS:boxcox'), and Kruskal's non-parametric test (R function 'kruskal.test') replaced ANOVA where no satisfactory data transformation could be found. Post-hoc testing was done with Tukey's test for ANOVA (function 'emmeans' from R package 'emmeans') and with Dunn's test (R function 'FSA:dunnTest') after Kruskal's test. Results are reported as means and their standard deviation (SD). The level of significance was set to $\alpha = 5\,\%$.

Results

During study conduct, the Covid pandemic and entailed social distancing measures substantially impeded and slowed recruitment and testing. In addition, lab space reservations ended in May 2021, so that we terminated the study at that time with 43 participants.

Anthropometric data

Groups were comparable with regards to body height, body weight and ASMM, and ASMM-index depicted a trend (p=0.068, Supplementary Table 1). Per selection criteria, age was different between young and old groups (p<0.001), but comparable within age groups. Body mass index was greater in OC than in YC (p=0.031, Figure 2A), and body fat

percentage was greater in OC than in all other groups (all p<0.001, Figure 2B). BIA phase angle, by contrast, was greater in YA than in all other groups (all p<0.001), and also greater in YC than in OC (p=0.011).

Structured exercise and habitual physical activity

As imposed by the inclusion criteria, athletes trained for more hours per week than control participants (Figure 3A), and the amount of weekly training was comparable between MA and YA. Actibelt adherence ranged between 11.6 and 18.1 h per day in individuals and was >14 h per day across groups, suggesting that representative data have been obtained. MA walked for greater time and distance, and they performed more walking steps than OC (all p<0.01, Supplementary Table 2). No group differences were found with regards to walking speed (p=0.84). However, stark group differences were found with regards to habitual running, with time, distance and step count all being greater in the athlete groups than in the control groups (all p<0.03). A

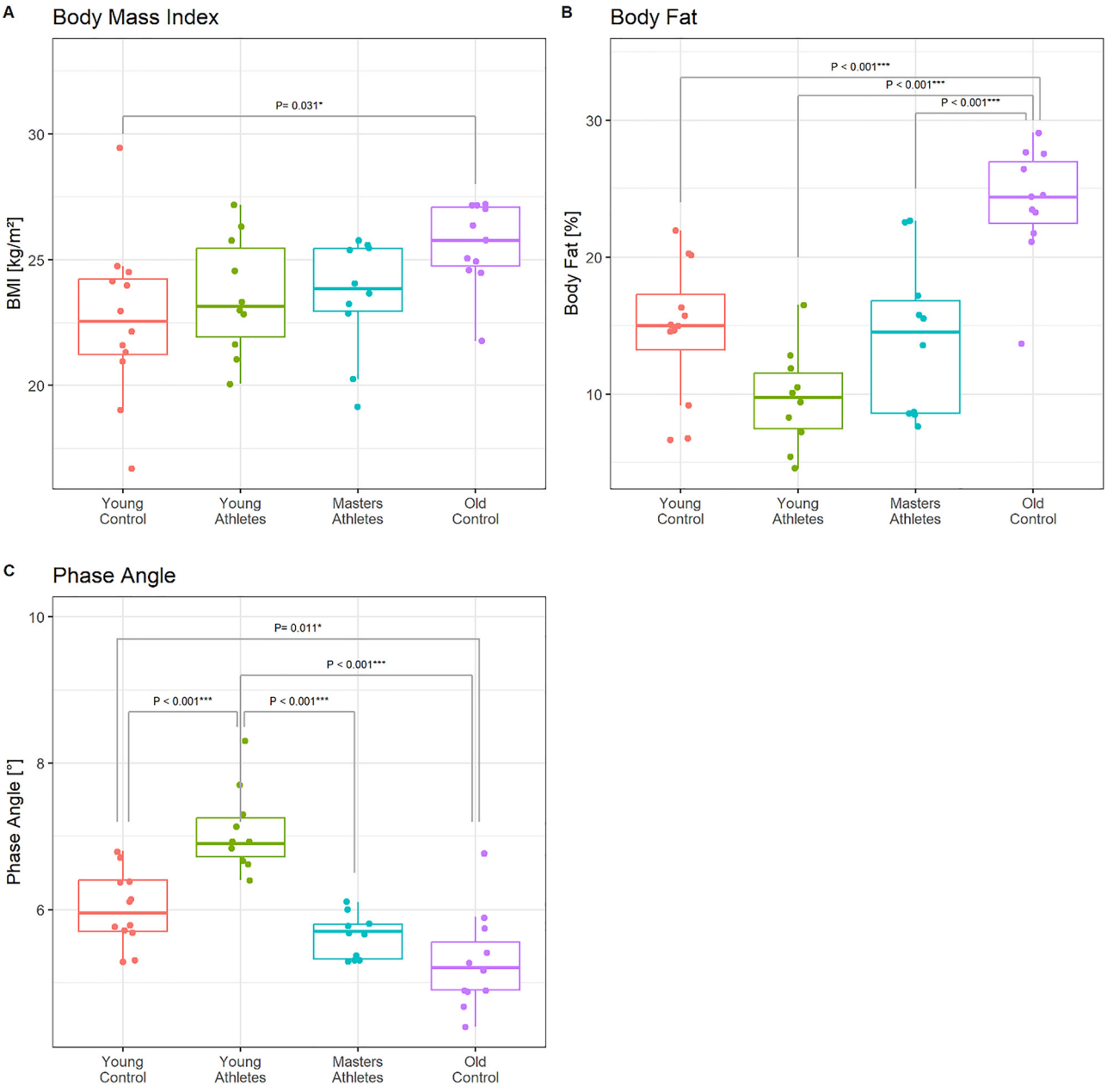

Figure 2: Body mass index (BMI), % body fat (from BIA), and whole body phase angle (assessed at 50 kHz), compared across groups.

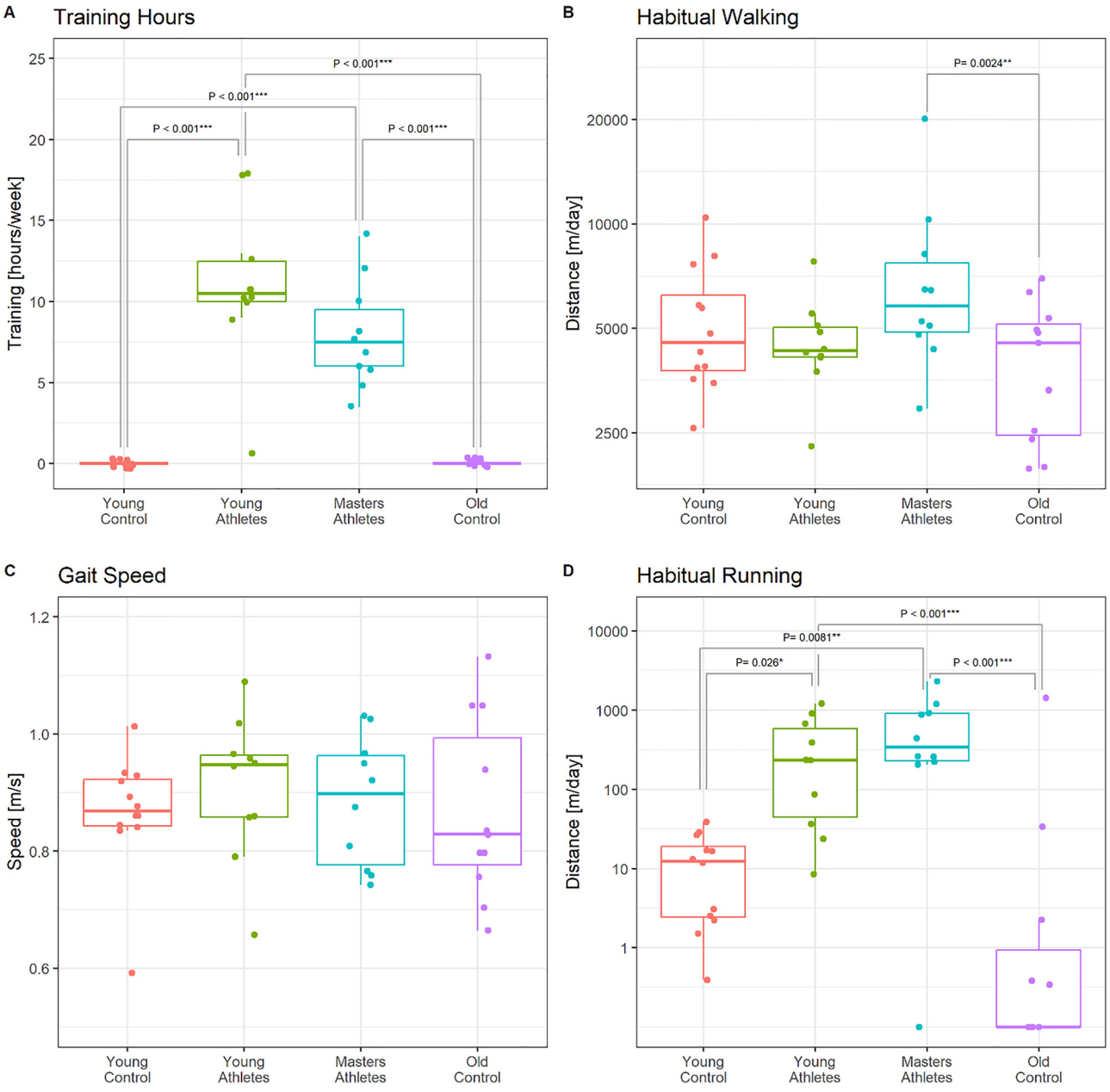

Figure 3: Training hours (assessed by questionnaire), habitual walking and running distance, as well as real-world gait speed, displayed across groups.

closer inspection revealed that control groups typically ran only over a few meters per day, whereas the athletes habitually ran several hundreds of meters (Figure 3C).

Cardiometabolic risk profile

Fasting glucose levels were greater in OC than in the young groups (both $p<0.01$, Figure 4), whereas HbA1c concentrations differed between young and old groups (all $p<0.05$). Insulin levels were more than twice as high in OC than in YC and MA (both $p<0.05$). HOMA-IR was greater in OC than in all other groups (all $p<0.01$). Of note, HOMA-IR was >2 in 6 out of 11 OC participants, i.e. suggestive of insulin resistance, but <2 in all participants of the other groups.

Group differences in markers of lipid metabolism were limited to triglyceride and total cholesterol levels (both $p<0.05$, Supplementary Table 3), which however failed to reveal significant post-hoc effects. Diastolic blood pressure and mean arterial pressure were found elevated by ~10 mmHg in OC as compared to YC and MA (all $p<0.05$), and systolic blood pressure was higher in OC than in YC ($p=0.027$).

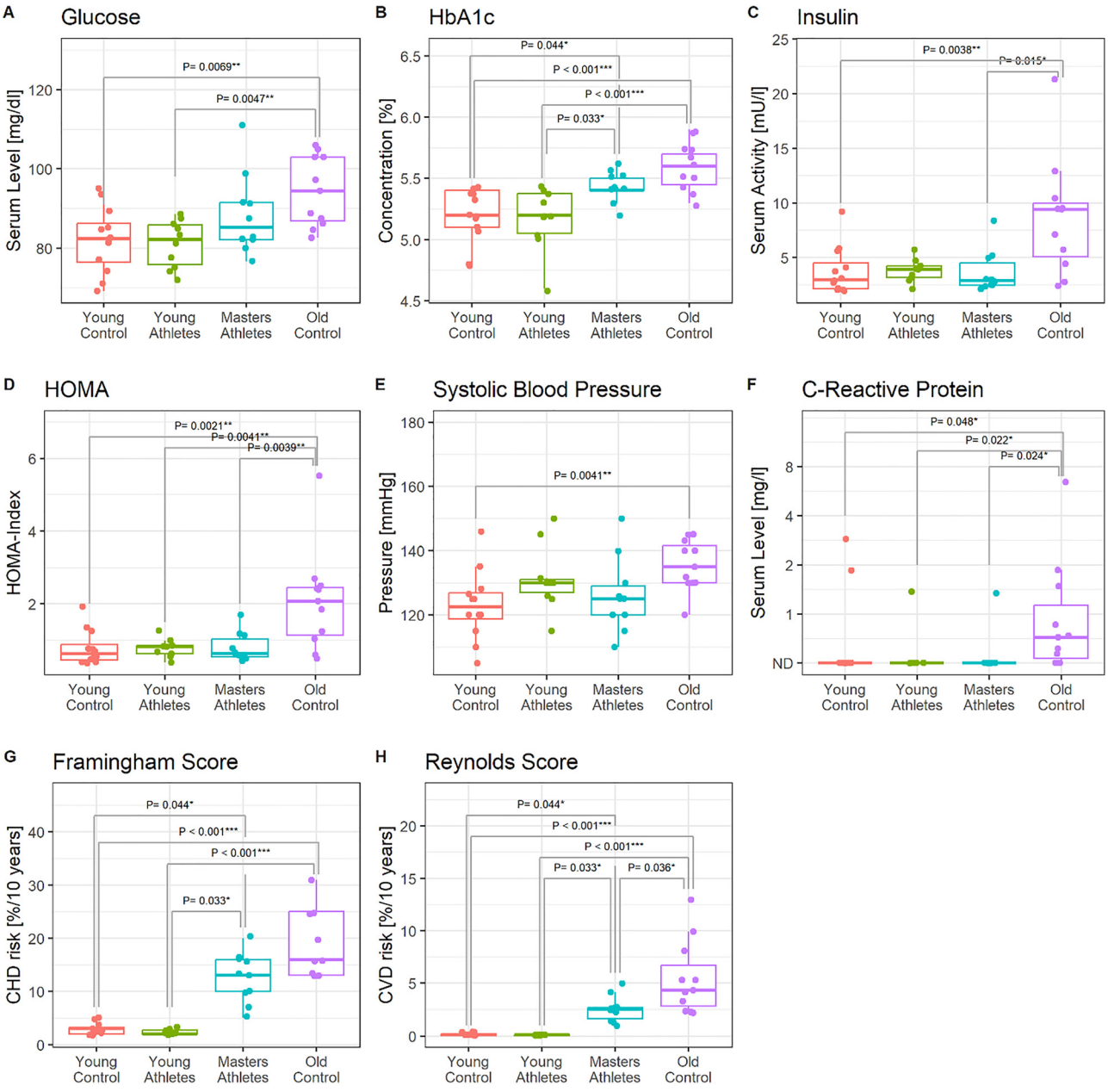

Figure 4: Markers of glucose metabolism, systolic blood pressure, C-reactive protein and the Framingham and Reynolds risk scores across groups. For CRP, non-detectable values (NA) were computer-coded to the smallest possible number so that they could be displayed on logarithmic scale.

C-reactive protein was below detection threshold only in 3 out of 32 participants (9.4 %) in YC, YA and MA, but in 8 out of 11 (73 %) of OC. Accordingly, CRP levels were higher in OC than in the other groups (all $p<0.05$).

The Framingham CHD risk score differed between young and old groups (all $p<0.001$). Although comparison between OC and MA suggested a risk reduction of (12.6/19.11–1) = –34 % in MA, this effect was not statistically significant ($p=0.26$). Finally, the Reynolds CVD risk score differed between young and old groups (all $p<0.001$), and it indicated a risk reduction between OC and MA by –54 % ($p=0.036$).

Discussion

This study has been the first to report on training and habitual physical activity in MA, and it is also the first to assess their cardiometabolic risk profile. Whilst body fat percentage best discriminated old control participants,

phase angle effectively discriminated young athletes from the other groups. The main difference regarding physical activity was that the athletes regularly trained and ran as part of their habitual routine, while the control groups, including the young participants, generally avoided running in their daily activities. Despite diabetes being an exclusion criterion for study participation, pronounced differences were found between groups with regards to glucose metabolism, whereas the more classical risk factors related to lipid metabolism and blood pressure showed small to moderate effects only.

Actimetry findings are remarkable in two ways. Firstly, it is surprising that real world gait speed did not reveal the effects of age and fitness that are often reported by other studies [33, 34]. This could be attributed to the relatively small sample size of the present study. However, it should also be considered that participants in this study were screened for good musculoskeletal health before inclusion into the study. This may have introduced a selection bias that contributed to the lack of age-related gait speed reductions in our study. Second, we were also surprised that the finding that athletes of either age group routinely run also outside their structured training, whilst non-physically active people almost never do. Although unknown to us, we speculate that the reasons why people habitually run comprise running after a train or bus, running after a person, or also running for pleasure. As much as the former assumption holds true, it would be a novel and surprising revelation that people who do not undertake structured physical activity do also tend to refrain from running within their habitual locomotion.

To date, the molecular contributors to inflammaging include various types of anti-pro-inflammatory molecules, particularly cytokines and chemokines [35, 36]. Among these, IL-6, IL-1β, and TNF-α play significant roles. In fact, these cytokines notably influence hepatocyte transcription among other cells, leading to increased release of CRP and other acute phase proteins, which are crucial in the body's response to infection [37]. CRP, in particular, may be recognized as a biomarker of inflammaging [38] and responds to anti-aging interventions [39]. In fact, our CRP findings suggest that MA are less prone to inflammaging than non-exercising older people.

The average serum CRP level in healthy Caucasians is <1 mg/dL. However, these baseline levels can significantly increase during infections to promote an adequate immune response. Our current work demonstrates the highest CRP levels in non-infected older individuals, while it notably shows low-normal levels in age-matched MA. This finding strongly suggests that improved body composition in combination with structured sprint- and jumping training can reduce CRP and likely also other inflammatory biomarkers. It also corroborates previous studies on anti-aging strategies involving caloric restriction [40] and physical exercise [41]. The correlation of CRP with cardiovascular risk is well-supported [42, 43], highlighting its role as a valuable biomarker for monitoring not only the aging process and cardiovascular/atherosclerosis diseases, but also anti-aging strategies.

In the present study we have chosen to use the Framingham CHD risk score, due to its high level of recognition. However, one has to realize that that risk score depends largely on age (which fully explains the significant results between young and old groups) and that it relies on blood pressure and serum lipids – variables that were only marginally affected in MA. Glucose metabolism and CRP, as a proposed marker of inflammaging, by contrast, did reveal pronounced beneficial effects in MA. The more recent Reynolds CVD score, by contrast, shows a weakly significant difference between MA and OC, suggesting that mitigation of cardiovascular risk in MA may act via decreased inflammaging levels. However, these results should be taken with a grain of salt, as risk predictions from the general population might not be directly transferrable to MA.

In the United States, nearly one-third of people aged 65 and older have diabetes, with prediabetes affecting almost 50 % of this group [44]. Both sedentary behavior as well as adiposity are risk factors for insulin resistance. Low physical activity levels are associated with an abnormal blood glucose profile in healthy adults [45]. Obesity and elevated body fat mass are independent risk factors for type 2 diabetes [46, 47]. As the OC had higher body fat mass besides lower physical activity levels, our study does not allow to discriminate the effects of fat mass and physical activity on glucose metabolism. However, only 1 MA, but 4 OC met the prediabetes criterion indicating impaired glucose tolerance with fasted serum glucose (≥100 mg/dL), and none of the MA, but 5 OC met the prediabetes criterion for HbA1c (≥5.7 %). Importantly, insulin resistance predisposes to macrovascular complications and is an important risk factor for cardiovascular disease [48], which possibly is inadequately covered by conventional risk scores. Although impaired glucose metabolism and insulin resistance are prevalent conditions in elderly individuals, improved body composition and structured training at high intensities may thus protect against metabolic diseases [49].

The limitations of this study lie firstly in its cross-sectional nature, and results may therefore be biased by secular effects and not reflect individual trajectories. However, such cross-sectional studies constitute a necessary first step before running costly and resource-consuming longitudinal studies. Another important limitation is the lack

of female participants, even though the risk of cardiovascular events is typically smaller in women than in men. Other limitations are the relatively small sample size, and that the data analysis was exploratory. Both limit the generalizability of the present results. However, that sample size was sufficiently large to address the primary hypothesis of the study (related to intramuscular connective tissue, will be reported elsewhere), and it has also been large enough to reveal traits in glucose metabolism and inflammaging in sufficient detail. Another limitation is the lack of a detailed account of all training activities. However, to give such an account is inherently difficult and beyond the scope of this paper. Furthermore, it would be desirable to have an in-depth analysis of the habitual running data, as it would be highly interesting to know the reasons why athletes seem to run habitually outside their structured training. However, even though this kind of analysis may be fruitful and is indeed intended in collaboration with the Trium company, we feel safe to infer differences between athlete vs. non-physically active groups. A further limitation relates to the problem of comparability between young athletes and MA. Whilst virtually all MA competed on international level, with several participants being international champions, most of the young athletes recruited to this study competed at national level only. However, international young athletes are typically professionals or semi-professionals, whereas MA are all amateurs. From that perspective, our recruitment of the athletic groups seems well justifiable. Further, our study only used standard assays for determination of CRP. Based on our findings, future studies should consider high-sensitivity kit, which allows quantitative analyses also with low-level concentrations. Finally, cardiometabolic risk may also be influenced by differences in nutrition and dietary habits, which we have not assessed in these cohorts.

Conclusions

In conclusion, our study demonstrates positive effects in sprint- and jump trained MA with regards to body composition, insulin sensitivity and inflammaging. These benefits were more pronounced for inflammaging and insulin sensitivity and must be expected to reflect improved cardiometabolic health, and thus lowering of the risk of cardiovascular events. In their classical study, Arem et al. report a 31 % reduction in cardiovascular risk for those who performed the equivalent of 7.5 h of vigorous physical activity [50]. This is not far off the ~8 h/week of training (mostly vigorous) plus ~2 h/week of walking (moderate activity), and this is in line with the 34 % risk reduction (Supplementary Table 2) when comparing the Framingham predictions between MA and OC. When using Reynolds' formula yields a 54 % risk reduction, which seems substantially larger. However, whether or not MA can indeed lower their cardiovascular risk to that extent has yet to be established. To that purpose, larger studies should be conducted that look into the dose-response curve for sprint and jump training, and also for other athletic specializations. For example, it would be feasible to replicate the assessment of the present paper in the wider context of a masters athletics field study, which could be hosted at their competition meetings. Another possibility would be to recruit older people before they start engaging in masters athletics and follow them up longitudinally.

Acknowledgments: We are thankful to our study participants – without their selfless contribution, this work would not have been possible. Special thanks go to Marcin Mider (Trium, Germany) for spot-on proofreading, and to Martin Daumer (Trium, Germany) for continued collaboration. Within this fruitful collaboration, we hope to be analyzing the accelerometry data in more depth in the future.

Research ethics: The study was ethically reviewed and approved by the Medical Council Northrhine-Westfalia (Landesärztekammer Nordrhein) with identifier 2018296. It was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and it was registered at the German clinical trials register (www.drks.de, registration no. DRKS00015764) before study commencement.

Informed consent: All participants gave their written informed consent prior to being included in the study.

Author contributions: Drafting manuscript: JR, MC, DP; conception: JR; study conduct: WS and JR; data processing and statistical analyses: JR. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Conflict of interest: The authors state no conflict of interest.

Research funding: The study was funded with internal funding from the DLR.

Data availability: The raw data will be uploaded with the manuscript.

References

1. Booth FW, Roberts CK, Thyfault JP, Ruegsegger GN, Toedebusch RG. Role of inactivity in chronic diseases: evolutionary insight and pathophysiological mechanisms. Physiol Rev 2017;97:1351–402.
2. Aggio D, Papachristou E, Papacosta O, Lennon LT, Ash S, Whincup P, et al. Trajectories of physical activity from midlife to old age and associations with subsequent cardiovascular disease and all-cause mortality. J Epidemiol Commun Health 2020;74:130.

3. Zhao M, Veeranki SP, Magnussen CG, Xi B. Recommended physical activity and all cause and cause specific mortality in US adults: prospective cohort study. BMJ 2020;370:m2031.
4. Stratton JR, Levy WC, Cerqueira MD, Schwartz RS, Abrass IB. Cardiovascular responses to exercise. Effects of aging and exercise training in healthy men. Circulation 1994;89:1648–55.
5. Guimarães GV, Ciolac EG, Carvalho VO, D'Avila VM, Bortolotto LA, Bocchi EA. Effects of continuous vs. interval exercise training on blood pressure and arterial stiffness in treated hypertension. Hypertens Res 2010;33:627–32.
6. Ghafari M, Faramarzi M, Baghurst T. Effect of exercise training on lipid profiles in the elderly: a systematic review and meta-analysis of randomized controlled trials. J Shahrekord Univ Med Sci 2020;22:200–7.
7. Solomon TP, Sistrun SN, Krishnan RK, Del Aguila LF, Marchetti CM, O'Carroll SM, et al. Exercise and diet enhance fat oxidation and reduce insulin resistance in older obese adults. J Appl Physiol (1985) 2008;104: 1313–19.
8. Pedersen BK. Muscle as a secretory organ. Compr Physiol 2013;3:1337–62.
9. Schuch FB, Vancampfort D, Richards J, Rosenbaum S, Ward PB, Stubbs B. Exercise as a treatment for depression: a meta-analysis adjusting for publication bias. J Psychiatr Res 2016;77:42–51.
10. Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, et al. Exercise training increases size of hippocampus and improves memory. Proc Natl Acad Sci USA 2011;108:3017–22.
11. Nilsson MI, Bourgeois JM, Nederveen JP, Leite MR, Hettinga BP, Bujak AL, et al. Lifelong aerobic exercise protects against inflammaging and cancer. PLoS One 2019;14:e0210863.
12. Franceschi C, Capri M, Monti D, Giunta S, Olivieri F, Sevini F, et al. Inflammaging and anti-inflammaging: a systemic perspective on aging and longevity emerged from studies in humans. Mech Ageing Dev 2007;128:92–105.
13. Franceschi C, Garagnani P, Morsiani C, Conte M, Santoro A, Grignolio A, et al. The continuum of aging and age-related diseases: common mechanisms but different rates. Front Med 2018;5:61.
14. Organization WH. Global recommendations on physical activity for health. Geneva: World Health Organization; 2010.
15. Davis MG, Fox KR. Physical activity patterns assessed by accelerometry in older people. Eur J Appl Physiol 2007;100:581–9.
16. Reaburn P, Dascombe B. Endurance performance in masters athletes. Euro Rev Aging Phys Act 2008;5:31–42.
17. Rittweger J, Kwiet A, Felsenberg D. Physical performance in aging elite athletes – challenging the limits of physiology. J Musculoskelet Neuronal Interact 2004;4:159–60.
18. Harridge SD, Lazarus NR. Physical activity, aging, and physiological function. Physiology 2017;32:152–61.
19. Tanaka H, Tarumi T, Rittweger J. Aging and physiological lessons from master athletes. Compr Physiol 2020;10:261–96.
20. Kontro TK, Bondarev D, Pyykönen K-M, von Bonsdorff M, Laakso L, Suominen H, et al. Motives for competitive sports participation in masters track and field athletes: impact of sociodemographic factors and competitive background. PLoS One 2022;17:e0275900.
21. Kontro TK, Sarna S, Kaprio J, Kujala UM. Mortality and health-related habits in 900 Finnish former elite athletes and their brothers. Br J Sports Med 2018;52:89–95.
22. Sanchez-Trigo H, Zange J, Sies W, Böcker J, Sañudo B, Rittweger J. Effects of aging and fitness on hopping biomechanics. Int J Environ Res Publ Health 2022;19:13696.
23. Chelly SM, Denis C. Leg power and hopping stiffness: relationship with sprint running performance. Med Sci Sports Exerc 2001;33:326–33.
24. Frey I, Berg A, Grathwohl D, Keul J. Freiburger Fragebogen zur körperlichen Aktivität – Entwicklung, Prüfung und Anwendung. Sozial-Präventivmed 1999;44:55–64.
25. Scorcelletti M, Zange J, Böcker J, Sies W, Lau P, Mittag U, et al. Associations between long-term exercise participation and lower limb joint and whole-bone geometry in young and older adults. Front Physiol 2023;14:1150562.
26. Sanchez-Trigo H, Rittweger J, Sañudo B. Effects of non-supervised exercise interventions on bone mineral density in adult women: a systematic review and meta-analysis. Osteoporos Int 2022;33: 1415–27.
27. Hoffmann K, Sallen J, Albert K, Richartz A. Zeitaufwendungen von Spitzensportlern in Leistungssport-und Bildungs-/Berufskarriere: Eine empirische Studie zum Zusammenhang mit chronischem Belastungserleben. Leipziger Sportwissenschaftliche Beiträge: Jahrgang *Heft 2* 2016. 2010;51:75.
28. Sergi G, De Rui M, Veronese N, Bolzetta F, Berton L, Carraro S, et al. Assessing appendicular skeletal muscle mass with bioelectrical impedance analysis in free-living Caucasian older adults. Clin Nutr 2015;34:667–73.
29. Keppler AM, Nuritidinow T, Mueller A, Hoefling H, Schieker M, Clay I, et al. Validity of accelerometry in step detection and gait speed measurement in orthogeriatric patients. PLoS One 2019;14: e0221732.
30. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation 1998;97:1837–47.
31. Ridker PM, Paynter NP, Rifai N, Gaziano JM, Cook NR. C-reactive protein and parental history improve global cardiovascular risk prediction: the Reynolds Risk Score for men. Circulation 2008;118:2243–51. 2244p following 2251.
32. Weber F, Stark C, Bloch W, Böcker J, Drey M, Gehlert S, et al. Therapeutic resistance training: proposal for an algorithm-based approach. Trans Exe Biomed 2024;1:89–101.
33. Grassi M, Von Der Straten F, Pearce C, Lee J, Mider M, Mittag U, et al. Changes in real-world walking speed following 60-day bed-rest. NPJ Microgravity 2024;10:6.
34. Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, et al. Gait speed and survival in older adults. JAMA 2011;305:50–8.
35. Li X, Li C, Zhang W, Wang Y, Qian P, Huang H. Inflammation and aging: signaling pathways and intervention therapies. Signal Transduct Targeted Ther 2023;8:239.
36. Capri M, Franceschi C, Salvioli S. Inflammaging targets. In: Rattan SIS, editor. Encyclopedia of Biomedical Gerontology. Oxford: Academic Press; 2020:271–8 pp.
37. Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. Front Immunol 2018;9:754.
38. Zhu Q, Zhang Q, Chen C, Liu M, He Y, Zhao Y, et al. C-reactive protein, neutrophil-to-lymphocyte ratio, and long-term mortality in Chinese centenarians. JAMA Netw Open 2023;6:e2340307.
39. Byrne T, Cooke J, Bambrick P, McNeela E, Harrison M. Circulating inflammatory biomarker responses in intervention trials in frail and sarcopenic older adults: a systematic review and meta-analysis. Exp Gerontol 2023;177:112199.
40. Fontana L, Meyer TE, Klein S, Holloszy JO. Long-term calorie restriction is highly effective in reducing the risk for atherosclerosis in humans. Proc Natl Acad Sci U S A 2004;101:6659–63.
41. Ford ES. Does exercise reduce inflammation? Physical activity and C-reactive protein among U.S. Adults. Epidemiology 2002;13:561–68.

42. Hebib L, Herraiz-Adillo Á, Higueras-Fresnillo S, Berglind D, Daka B, Wennberg P, et al. Life's Essential 8 is inversely associated with high-sensitivity C-reactive protein. Sci Rep 2024;14:15024.
43. Neumann JT, Twerenbold R, Weimann J, Ballantyne CM, Benjamin EJ, Costanzo S, et al. Prognostic value of cardiovascular biomarkers in the population. JAMA 2024;331:1898–909.
44. National diabetes statistics report. [https://www.cdc.gov/diabetes/php/data-research/index.html].
45. Mainous AG, 3rd, Tanner RJ, Anton SD, Jo A, Luetke MC. Physical activity and abnormal blood glucose among healthy weight adults. Am J Prev Med 2017;53:42–7.
46. Sun J, Liu Z, Zhang Z, Zeng Z, Kang W. The correlation of prediabetes and type 2 diabetes with adiposity in adults. Front Nutr 2022;9:818263.
47. Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature 2006;444:840–6.
48. Bonora E, Kiechl S, Willeit J, Oberhollenzer F, Egger G, Meigs JB, et al. Insulin resistance as estimated by homeostasis model assessment predicts incident symptomatic cardiovascular disease in caucasian subjects from the general population: the bruneck study. Diabetes Care 2007;30:318–24.
49. Lin J, Zhang X, Sun Y, Xu H, Li N, Wang Y, et al. Exercise ameliorates muscular excessive mitochondrial fission, insulin resistance and inflammation in diabetic rats via irisin/AMPK activation. Sci Rep 2024;14:10658.
50. Arem H, Moore SC, Patel A, Hartge P, Berrington de Gonzalez A, Visvanathan K, et al. Leisure time physical activity and mortality: a detailed pooled analysis of the dose-response relationship. JAMA Intern Med 2015;175:959–67.

Supplementary Material: This article contains supplementary material (https://doi.org/10.1515/teb-2024-0021).