Nutrition 126 (2024) 112516

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

Iron deficiency in athletes: Prevalence and impact on VO_2 peak

Karsten Keller M.D. [a,b,c,*], Oliver Friedrich M.Sc. [a], Julia Treiber B.A. [a], Anne Quermann M.Sc. [a], Birgit Friedmann-Bette M.D. [a]

[a] Department of Sports Medicine, Medical Clinic VII, University Hospital Heidelberg, Heidelberg, Germany
[b] Department of Cardiology, University Medical Center of the Johannes Gutenberg-University Mainz, Mainz, Germany
[c] Center for Thrombosis and Hemostasis (CTH), University Medical Center of the Johannes Gutenberg-University Mainz, Mainz, Germany

ARTICLE INFO

Article History:
Received 12 February 2024
Received in revised form 4 June 2024
Accepted 6 June 2024

Keywords:
Iron deficiency
Athletic performance
Anemia
Spiroergometry
Sport activity

ABSTRACT

Background: Iron is an important micronutrient in pathways of energy production, adequate nutrient intake and its balance is essential for optimal athletic performance. However, large studies elucidating the impact of iron deficiency on athletes' performance are sparse.
Methods: Competitive athletes of any age who presented for preparticipation screening 04/2020–10/2021 were included in this study and stratified for iron deficiency (defined as ferritin level <20 µg/l with and without mild anemia [hemoglobin levels ≥11 g/dl]). Athletes with and without iron deficiency were compared and the impact of iron deficiency on athletic performance was investigated.
Results: Overall, 1190 athletes (mean age 21.9 ± 11.6 years; 34.2% females) were included in this study. Among these, 19.7% had iron deficiency. Patients with iron deficiency were younger (18.1 ± 8.4 vs. 22.8 ± 12.1 years, $P < 0.001$), more often females (64.5% vs. 26.8%, $P < 0.001$), had lower VO_2 peak value (43.4 [38.5/47.5] vs. 45.6 [39.1/50.6]ml/min/kg, $P = 0.022$) and lower proportion of athletes reaching VO_2 peak of >50 ml/min/kg (8.5% vs. 16.1%, $P = 0.003$). Female sex (OR 4.35 [95% CI 3.13–5.88], $P > 0.001$) was independently associated with increased risk for iron deficiency. In contrast, the risk for iron deficiency decreased by every life year (OR 0.97 [95% CI 0.95–0.99], $P = 0.003$). Iron deficiency was independently associated with reduced VO_2 peak (OR 0.94 [0.91–0.97], $P < 0.001$) and lower probability to reach VO_2 peak >50 ml/min/kg (OR 0.42 [95% CI 0.25–0.69], $P = 0.001$).
Conclusions: Iron deficiency is common in athletes (predominantly in female and in young athletes). Iron deficiency was independently associated with reduced VO_2 peak during exercise testing and lower probability to reach a VO_2 peak >50 ml/min/kg.

Introduction

Iron deficiency with and without anemia is a global health problem, which is commonly detected in daily clinical practice [1–3]. Iron deficiency is a leading contributor to the global burden of disease affecting particularly children, premenopausal women, and people, who live in low-income and middle-income countries [1–3].

Iron deficiency progresses in three consecutive stages. In the first stage only the iron stores in reticulo-endothelial cells of the bone marrow, liver and spleen are depleted, referred as iron storage depletion, accompanied by a fall of serum ferritin [1–4]. The second stage comprises decreased transport iron and is afflicted by reduced iron supply to the cells with a decreased transferrin saturation [1–4]. These two first stages of iron deficiency without anemia were referred as pre-anemic latent iron deficiency or as iron deficient non-anemia [1–4]. The last stage of iron deficiency is characterized by fall of hemoglobin synthesis caused by insufficient iron supply resulting in anemia [1–4].

Iron is crucial for physiological (biological) functions of the human body, including in particular the respiratory and the blood cell system with focus on the oxygen transport, energy production, DNA synthesis, and also cell proliferation [1,2]. Iron deficiency refers to reduced iron stores that may lead to overt anemia or persist without further progression [1,2].

While in developing countries iron deficiency is most often caused by insufficient dietary intake, loss of blood due to intestinal worm colonization or a combination of both, in high-income countries, increasing frequencies regarding eating habits (especially

*Corresponding author.
E-mail address: karsten.keller@med.uni-heidelberg.de (K. Keller).

https://doi.org/10.1016/j.nut.2024.112516
0899-9007/

vegan, vegetarian diet or no eating of red meat), pathological conditions such as chronic blood loss or malabsorption in the light of the aging populations are the main drivers of iron deficiency [1,2].

Anemia is the main consequence of iron deficiency besides many other consequences, but clinical and functional impairments driven by iron deficiency can already occur in the absence of anemia [3]. Iron deficiency is frequently identified in endurance athletes resulting from hemolysis, blood loss and mild inflammation in the light of prolonged training and repeated ground contacts, causing iron loss through several potential mechanisms [1,5–8]. Additional factors are iron losses due to sweating, hematuria and gastrointestinal (micro) bleeding, hemodilution, redistribution, increased iron demands, decreased absorption, increased losses, and sequestration, in combination with genetic determinants (of different types of anemia) [8–10]. Studies suggesting also an association between vitamin D and iron status [11–14].

Iron is an important functional component of oxygen transport and energy production in humans as well as a critical and essential micronutrient for athletes‘ excellent sport-performance [4]. While it is well known that iron deficiency anemia is strongly related to reduced athletic performance [6,15–17], impact of iron deficiency with or without mild anemia on the athletic performance is less clear and study results are contradictory [18,19]. Large studies elucidating the impact of iron deficiency on athletes’ performance are sparse. Thus, we aimed to investigate the impact of iron deficiency with or without mild anemia on athletes’ performance in our large study sample.

Methods

We performed a retrospective analysis of data routinely collected on athletes of any age presenting at our Department of Sports Medicine (Medical Clinic VII) of the University Hospital Heidelberg (Germany) for their preparticipation screening examination between April 2020 and October 2021. This is a secondary analysis of data collected for a previously published study evaluating blood pressure in athletes [20]. However, the cohort size was large enough to address other important objectives like the impact of iron deficiency on athletic performance.

Enrolled subjects

Athletes were eligible for inclusion in this study, if they performed a regular training for competition and presented for preparticipation screening examination or post-COVID-19 return-to-sport-testing and had a ferritin laboratory result on the examination day [20–24].

Ethical aspects

The requirement for athletes’ informed consent for this study was waived as we used only anonymized retrospective data routinely collected during the health screening examination process. Studies in Germany involving a retrospective analysis of diagnostic standard data of anonymous patients after anonymization do not require an ethics statement, in accordance with German law/legacy.

Definitions and assessed parameters

In the literature and guidelines, cut-off values of ferritin ranging between 15 and 45 μg/l are recommended to diagnose iron deficiency in patients with anemia [1–3,8,25–28]. In accordance with some studies and recommendations [8,14,18,29], we have chosen a ferritin level of ≤ 20 μg/l to define an iron deficiency in female and male athletes for our study. Since we wanted to include only patients with normal or slightly reduced hemoglobin levels, patients with hemoglobin levels <11 g/dl were excluded from the study.

In all included and investigated athletes of this study, transthoracic echocardiography was performed. Echocardiographic parameters were defined according to current guidelines [22,30].

Exercise testing was performed according to current guidelines with continuously recorded electrocardiogram (ECG) and repeated BP measurements at the end of every load level. The exercise test was stopped if the athlete was at his maximum capacity or stopping criteria according to current guidelines enforced the stop of the exercise testing [21,22].

Statistics

The included athletes were stratified for presence of iron deficiency and athletes with and without iron deficiency were compared using the Wilcoxon-Mann-Whitney-U-Test for continuous variables and Fisher’s exact or chi^2 test for categorical variables, as appropriate. Data of continuous variables were presented as median and interquartile range and categorical variables as absolute numbers with related percentages.

We performed univariate and multivariate logistic regression models to investigate associations between different patient characteristics on the one hand and presence of iron deficiency on the other hand. In addition, univariate and multivariate logistic regression models were computed to investigate the impact of iron deficiency on exercise parameters and especially on VO_2 peak values during exercise testing and VO_2 peak >50 ml/min/kg. Multivariate regression models were adjusted for age and BMI in order to proof the independence of the statistical results of these known influencing parameters. Results of the logistic regressions are presented as odds ratio (OR) and 95% confidence interval (CI).

All of the statistical analyses were calculated with the use of SPSS software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY, USA). Only the P values < 0.05 (two-sided) were considered to be statistically significant. No adjustment for multiple testing was applied for the present analysis.

Results

Overall, 1190 athletes (mean age 21.9 ± 11.6 years; 407 [34.2%] females) were included in the present study between April 2020 and October 2021. Among the included patients, 19.7% had an iron deficiency with and without mild anemia (Table 1).

Iron deficiency occurred more often in female athletes and in younger age, especially in the first two decades of life (Fig. 1).

Comparison of athletes with and without iron deficiency

Patients with iron deficiency were younger (18.1 ± 8.4 vs. 22.8 ± 12.1 years, $P < 0.001$), more often females (64.5% vs. 26.8%, $P < 0.001$), had lower BMI (21.0 [19.7/22.7] vs. 23.0 [21.0/25.0] kg/m^2, $P < 0.001$) in the light of higher body fat (15.8 [9.4/18.5] vs. 10.8 [8.5/15.3] %, $P < 0.001$) (Table 1).

Exercise parameters revealed lower VO_2 peak value (43.4 [38.5/47.5] vs. 45.6 [39.1/50.6] ml/min/kg, $P = 0.022$) and correspondingly lower proportion of athletes reaching VO_2 peak of >50 ml/min/kg (8.5% vs. 16.1%, $P = 0.003$) in these with iron deficiency

Table 1
Patients' characteristics of the 1190 examined athletes stratified for iron deficiency

Parameters	Athletes without iron deficiency (*N* = 956; 80.3%)	Athletes with iron deficiency (*N* = 234; 19.7%)	*P*-value
Age (in years)	22.8 ± 12.1	18.1 ± 8.4	< **0.001**
Female sex	256 (26.8%)	151 (64.5%)	< **0.001**
Body height (cm)	177.0 (169.0/183.0)	168.0 (162.0/175.0)	< **0.001**
Body weight (kg)	72.1 (62.2/81.5)	61.1 (53.9/67.5)	< **0.001**
Body mass index (kg/m^2)	23.0 (21.0/25.0)	21.0 (19.7/22.7)	< **0.001**
Body fat (%)	10.8 (8.5/15.3)	15.8 (9.4/18.5)	< **0.001**
Leading athletes of a regional and national level	704 (73.6%)	172 (73.5%)	0.966
Former SARS-CoV-2-infection	146 (15.3%)	10 (4.3%)	< **0.001**
Cardiovascular risk factors			
Nicotine abuse	37 (3.9%)	2 (0.9%)	**0.022**
Obesity*	21 (2.2%)	1 (0.4%)	0.072
Exercise parameters			
VO_2 peak (ml/min/kg)	45.6 (39.1/50.6)	43.4 (38.5/47.5)	**0.022**
VO_2 peak > 50 ml/min/kg	154 (16.1%)	20 (8.5%)	**0.003**
Maximal respiratory exchange ratio (RER)	1.15 (1.11/1.21)	1.15 (1.09/1.19)	0.155
Maximal respiratory exchange ratio (RER) > 1.1	408 (42.7%)	84 (35.9%)	0.059
Maximum lactate value	9.53 (7.96/11.34)	8.42 (7.45/10.41)	**0.009**
Echocardiographic parameters			
Left ventricular ejection fraction measured by Simpson method (%)	65.0 (62.0/69.0)	65.0 (62.0/69.0)	0.294

P values < 0.05 were considered to be statistically significant.
*Obesity was defined as body mass index (BMI) ≥ 30 kg/m^2 according to the standards of the World Health Organization (WHO) [20,47,48].

compared to those without, despite similar exhaustion levels (Table 1, Fig. 2A and 2B).

Left ventricular ejection fraction was comparable between both groups (Table 1).

Associated factors with iron deficiency

Female sex (OR 4.35 [95% CI 3.13–5.88], $P > 0.001$) and higher body-fat (OR 1.16 [95% CI 1.12–1.20], $P < 0.001$) were independently associated with increased risk for iron deficiency (Table 2). In contrast, the risk for iron deficiency decreased by every life year (OR 0.97 [95% CI 0.95–0.99], $P = 0.003$) and with higher BMI (OR 0.85 [95% CI 0.81–0.90], $P < 0.001$). Former SARS-CoV2-infection was associated with lower prevalence of iron deficiency (OR 0.30 [95% CI 0.16–0.59], $P < 0.001$) (Table 2).

Impact of iron deficiency on athletic performance

Iron deficiency was independently associated with reduced VO_2 peak values during exercise testing (OR 0.94 [0.91–0.97], $P < 0.001$) and lower probability to reach a VO_2 peak >50 ml/min/kg (OR 0.42 [95% CI 0.25–0.69], $P = 0.001$) (Table 3, Fig. 2C), whereas maximal respiratory exchange ratio (RER) was not affected and not different between both groups ($P = 0.435$). The impact of iron deficiency was detected in both, athletes with full physical exertion (defined as maximal respiratory exchange ratio [RER] > 1.10) with

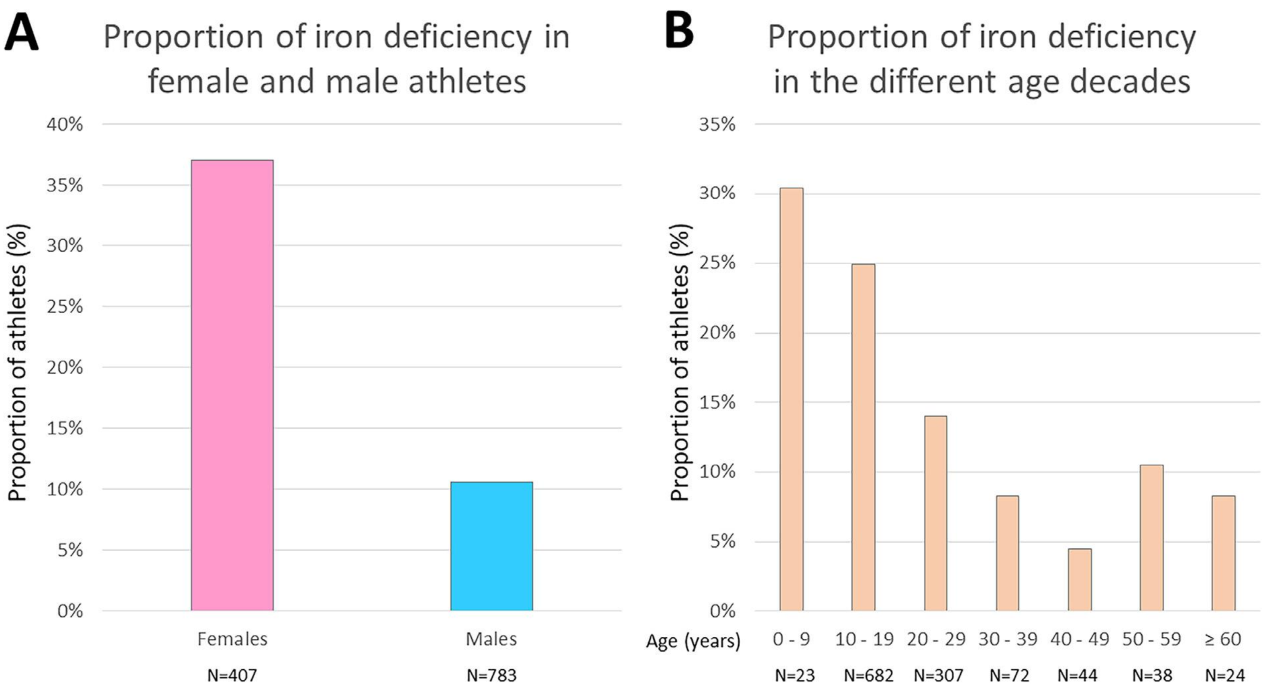

Fig. 1. Proportions of iron deficiency in female and male athletes (panel A) and in the different age decade (panel B). Iron deficiency was defined by ferritin level of ≤20 µg/l.

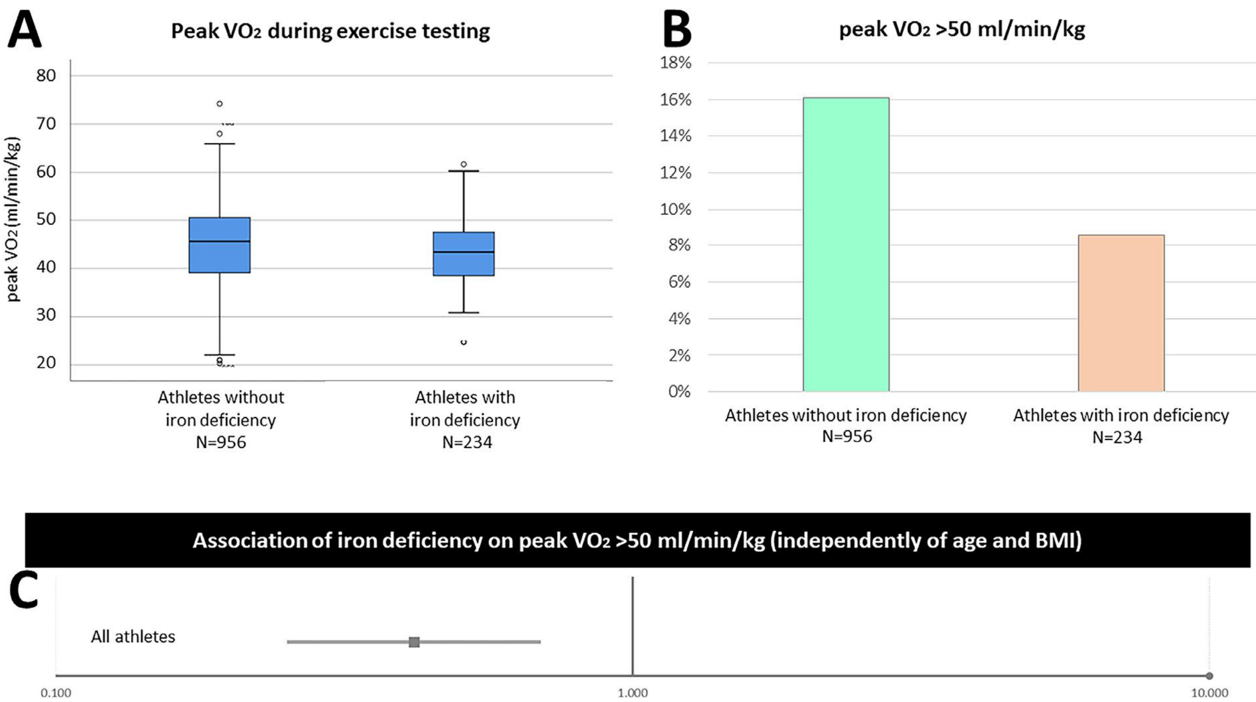

Fig. 2. Impact of iron deficiency on peak VO_2 values during exercise testing; Panel A—Comparison peak VO_2 in athletes with and without iron deficiency; Panel B—Proportion of peak $VO_2 > 50$ ml/min/kg in athletes stratified for iron deficiency; Panel C—Association of iron deficiency with $VO_2 > 50$ ml/min/kg (Iron deficiency was defined by ferritin level of $\leq 20 \mu g/l$).

an OR adjusted for age and BMI of 0.40 (95% CI 0.22–0.73, $P = 0.003$) and in those athletes with a RER $\leq$ 1.10 showing also an independent association of iron deficiency with reduced VO_2 peak values during exercise testing after adjustment for age and BMI (OR 0.34 [95% CI 0.12–0.99], $P = 0.049$).

Discussion

Although iron deficiency is an often identified phenomenon in athletes and especially in those of female sex, data about the impact of iron deficiency with and without mild anemia on athletic performance is contradictory [18,19]. Thus, the main objective of this study was to investigate whether iron deficiency with and without mild anemia (hemoglobin levels $\geq$ 11 g/dl) had a significant impact on athletes' performance.

The key results of our study could be summarized as follows:

1. Approximately 1/5 of the athletes were afflicted with iron deficiency.
2. Female sex as well as younger age were associated with iron deficiency.
3. Reduced athletic performance comprising VO_2 peak value and lower proportion of athletes reaching VO_2 peak of >50 ml/min/kg was related to iron deficiency.
4. Iron deficiency was independently associated with reduced VO_2 peak values during exercise testing and lower probability to reach an VO_2 peak >50 ml/min/kg.

Iron deficiency is a commonly encountered condition among athletes [19,31,32]. In our study, approximately 20% of all athletes and more than 35% of the female athletes had iron deficiency. Our

Table 2
Association of different factors with iron deficiency (univariate and multivariate logistic regression model)

	Iron deficiency			
	Univariate regression model		Multivariate regression model (adjusted for age and BMI)	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age (in years)	0.95 (0.93–0.97)	< **0.001**	0.97 (0.95–0.99)	**0.003**
Male sex	0.20 (0.15–0.27)	< **0.001**	0.23 (0.17–0.32)	< **0.001**
Body mass index (kg/m²)	0.82 (0.78–0.86)	< **0.001**	0.85 (0.81–0.90)	< **0.001**
Body fat (%)	1.12 (1.08–1.15)	< **0.001**	1.16 (1.12–1.20)	< **0.001**
Former SARS-CoV-2-infection	0.25 (0.13–0.48)	< **0.001**	0.30 (0.16–0.59)	< **0.001**
Cardiovascular risk factors				
Nicotine abuse	0.21 (0.05–0.90)	**0.035**	0.50 (0.11–2.18)	0.354
Obesity*	0.19 (0.03–1.43)	0.107	0.34 (0.04–2.59)	0.297
Echocardiographic parameters				
Left ventricular ejection fraction measured by Simpson method (%)	1.01 (0.98–1.05)	0.367	1.02 (0.98–1.05)	0.329

P values < 0.05 were considered to be statistically significant.
*Obesity was defined as body mass index (BMI) $\geq$ 30 kg/m² according to the standards of the World Health Organization (WHO) [20,47].

Table 3
Association of iron deficiency with performance measures (univariate and multivariate logistic regression model)

	Iron deficiency			
	Univariate regression model		Multivariate regression model (adjusted for age and BMI)	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
VO_2 peak	0.98 (0.95–1.00)	0.068	0.94 (0.91–0.97)	< **0.001**
VO_2 peak > 50 ml/min/kg	0.49 (0.30–0.79)	**0.004**	0.42 (0.25–0.69)	**0.001**
Maximal respiratory exchange ratio (RER)	0.12 (0.01–1.79)	0.124	0.32 (0.02–5.56)	0.435
Maximal respiratory exchange ratio (RER) > 1.1	0.75 (0.56–1.01)	0.060	0.98 (0.72–1.34)	0.921

P values < 0.05 were considered to be statistically significant.

results agree with those of Roy et al. who reported iron deficiency in 10.9% of males and 35.9% of female athletes [32]. In contrast, Sandström et al. reported an even higher proportion of athletes with iron deficiency (52%) of the female senior high school top-level athletes [19,31]. In line with literature [4,19,31–33] our study demonstrated that iron deficiency was substantially more prevalent in female as well as adolescent athletes [4,11,29–31]. Regarding age, our study is in line with previously published studies, showing highest proportion of iron deficiency in athletes in the age-group <19 years [32].

Regarding gender-differences, females' iron losses via menstruation and lower iron intake compared to male athletes are the most likely reasons why female athletes had higher prevalence of iron deficiency [16,19,32]. Another important cause of iron deficiency in athletes might be the usage of non-steroidal anti-inflammatory drugs (NSAIDs), which may increase the risk for bleeding [33].

The negative influence of iron deficiency anemia on physical work capacities is established since several decades [6,15,16,34,35]. Studies have proven, that iron deficiency anemia had a substantial impact on physical working capacity and athletic performance [6,15,16,34,35]. The impact of iron deficiency with or without mild anemia is less clear and results are contradictory [18,19,36].

Our study demonstrated that iron deficiency was significantly related to reduced athletic performance comprising VO_2 peak value and to a lower proportion of athletes reaching VO_2 peak of >50 ml/min/kg. This finding was independent of age and BMI in the adjusted multivariate regression analyses. These results are in part in accordance with literature [37,38]. Dellavalle et al reported that rowers with normal iron status trained approximately 10 min more per day than rowers with depleted iron (P = 0.02). In addition, rowers with iron deficiency had a lower VO_2 peak (P = 0.03) regardless of training intensity [37]. The study of Pate et al. reported a significant negative associations between serum ferritin and running activity in female runners ($P < 0.05$) [38]. Moreover, animal experiments conducted with rats that were fed a low iron diet showed similarly a lower maximum oxygen uptake and increased muscle fatigue in animals with iron deficiency [39].

In contrast, other studies failed to confirm a relationship between iron deficiency or mild iron deficiency anemia on reduced performance [36,40]. Celsing reported that an artificial induced iron deficiency did not affect endurance in healthy male subjects without anemia [40]. Additionally, Tsai et al. detected no association between mild anemia and 2-minute sit-ups performance [36]. The authors concluded that unspecified mild anemia might only be associated with reduced cardiorespiratory fitness but not with decreased anaerobic fitness [36].

In this context, iron-dependent metabolic pathways comprise on the one hand hemoglobin and myoglobin for oxygen transport and on the other hand oxidative production of adenosine triphosphate for muscle contraction [10,19,41]. Thus, iron deficiency is typically primarily related to impaired aerobic performance with increasing performance loss driven by growing iron deficiency anemia [6,15,16,34,35,41–43]. However, since oxygen transport capacities are unchanged in iron deficiency without anemia, the reason for impaired athletic performance in iron deficiency without anemia is not well elucidated [19,41]. Impaired function of oxidative enzymes and respiratory proteins might play a key role in respect of reduced athletic performance driven by iron deficiency without anemia [6,17,19,41]. However, the relationship between the iron status and athletic performance is complex and important to note bidirectional [9]. Several mechanisms may contribute to this reduced athletic performance in iron-deficient athletes [9,39]. In animal models, iron deficiency was associated with lower levels of hemoglobin, cytochrome c, cytochrome oxidase, and mitochondrial glycerol-3-phosphate dehydrogenase activity, which may be related to impaired cellular respiration and metabolism [9,39]. Reduced oxygen availability caused by iron deficiency might necessitate greater reliance on anaerobic metabolism and therefore result in increased lactate concentrations, reduced glycogen levels as well as lower blood pH, and (earlier) depletion of muscle glycogen [9,44]. Iron deficiency is additionally connected with decreased numbers of mitochondria, reduced muscle activities of myoglobin, succinate dehydrogenase, and cytochrome c, reinforcing reduced exercise capacities and reduced athletic performance [9,39].

It is important to mention that the recommendations for the dietary intake of iron for males and premenopausal females do not take the augmented iron demands attributable to exercise/sports into account [9,45]. It is well known that athletes, especially endurance athletes, may have an iron demand exceeding the recommended iron intake by 70% per day [9,45]. However, studies revealed that iron supplementation in athletes without iron deficiency does not improve their endurance performance [18,41]. Largest benefit regarding increased athletic performance was detected in athletes with iron deficiency with lowered ferritin levels < 20 µg/l [17,18]. In this context, it has to be mentioned that evolving evidence suggest that already iron deficiency without anemia might have a long-term impact on mental, psychomotor, and behavioral development in children and adolescent individuals [46].

Awareness by sports medicine physicians regarding iron deficiency in athletes is still not sufficiently developed [16]. While the Centers for Disease Control and Prevention in the United States recommended screening of all non-pregnant women for anemia every 5–10 years throughout their childbearing life-years, the National Athletic Trainers' Association does not currently recommend anemia screening in asymptomatic athletes [16].

However, iron deficiency occurs in athletes participating in a wide spectrum of sport disciplines and at any age (from childhood to senior athletes). The high prevalence of iron deficiency and its impact on adequate development in childhood and adolescence [46] as well as on athletic performance, underline the outstanding importance of screening examinations regarding iron deficiency to avoid both, health deviations as well as reduced or stagnant performance levels in sports [8].

Limitations

There are certain limitations of our study which need to be mentioned: First, the main limitation of our study is the single-center retrospective study design. Second, no adjustments for multiple testing was conducted. Third, due to the retrospective study design, we were not able to analyze the effect of infections on ferritin levels.

Conclusions

Iron deficiency is common in athletes (predominantly in female and young athletes). Iron deficiency was independently associated with reduced VO_2 peak values during exercise testing and lower probability to reach VO_2 peak levels >50 ml/min/kg.

Declaration of competing interest

KK, OF, JT, AQ, and BFB report no conflict of interests.

CRediT authorship contribution statement

Karsten Keller: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Oliver Friedrich:** Writing – review & editing. **Julia Treiber:** Writing – review & editing. **Anne Quermann:** Writing – review & editing. **Birgit Friedmann-Bette:** Writing – review & editing.

References

[1] Camaschella C. Iron-deficiency anemia. N Engl J Med 2015;373(5):485–6. https://doi.org/10.1056/NEJMc1507104.
[2] Camaschella C. Iron deficiency. Blood 2019;133(1):30–9. https://doi.org/10.1182/blood-2018-05-815944.
[3] Pasricha SR, Tye-Din J, Muckenthaler MU, Swinkels DW. Iron deficiency. Lancet 2021;397(10270):233–48. https://doi.org/10.1016/S0140-6736(20)32594-0.
[4] Alaunyte I, Stojceska V, Plunkett A. Iron and the female athlete: a review of dietary treatment methods for improving iron status and exercise performance. J Int Soc Sports Nutr 2015;12:38. https://doi.org/10.1186/s12970-015-0099-2.
[5] Burden RJ, Pollock N, Whyte GP, Richards T, Moore B, Busbridge M, et al. Effect of intravenous iron on aerobic capacity and iron metabolism in elite athletes. Med Sci Sports Exerc 2015;47(7):1399–407. https://doi.org/10.1249/MSS.0000000000000568.
[6] Beard J, Tobin B. Iron status and exercise. Am J Clin Nutr 2000;72(2 suppl):594S–7S. https://doi.org/10.1093/ajcn/72.2.594S.
[7] Telford RD, Sly GJ, Hahn AG, Cunningham RB, Bryant C, Smith JA. Footstrike is the major cause of hemolysis during running. J Appl Physiol (1985) 2003;94(1):38–42. https://doi.org/10.1152/japplphysiol.00631.2001.
[8] Damian MT, Vulturar R, Login CC, Damian L, Chis A, Bojan A. Anemia in sports: a narrative review. Life (Basel) 2021;11(9):987. https://doi.org/10.3390/life11090987.
[9] Kardasis W, Naquin ER, Garg R, Arun T, Gopianand JS, Karmakar E, et al. The IRONy in athletic performance. Nutrients 2023;15(23):4945. https://doi.org/10.3390/nu15234945.
[10] Abbaspour N, Hurrell R, Kelishadi R. Review on iron and its importance for human health. J Res Med Sci 2014;19(2):164–74 https://www.ncbi.nlm.nih.gov/pubmed/24778671.
[11] Malczewska-Lenczowska J, Sitkowski D, Surala O, Orysiak J, Szczepanska B, Witek K. The association between iron and vitamin d status in female elite athletes. Nutrients 2018;10(2):167. https://doi.org/10.3390/nu10020167.
[12] Shoemaker ME, Salmon OF, Smith CM, Duarte-Gardea MO, Cramer JT. Influences of vitamin d and iron status on skeletal muscle health: a narrative review. Nutrients 2022;14(13):2717. https://doi.org/10.3390/nu14132717.
[13] Azizi-Soleiman F, Vafa M, Abiri B, Safavi M. Effects of iron on vitamin d metabolism: a systematic review. Int J Prev Med 2016;7:126. https://doi.org/10.4103/2008-7802.195212.
[14] Solberg A, Reikvam H. Iron status and physical performance in athletes. Life (Basel) 2023;13(10):2007. https://doi.org/10.3390/life13102007.
[15] Gardner GW, Edgerton VR, Senewiratne B, Barnard RJ, Ohira Y. Physical work capacity and metabolic stress in subjects with iron deficiency anemia. Am J Clin Nutr 1977;30(6):910–7. https://doi.org/10.1093/ajcn/30.6.910.
[16] Myhre KE, Webber BJ, Cropper TL, Tchandja JN, Ahrendt DM, Dillon CA, et al. Prevalence and impact of anemia on basic trainees in the US air force. Sports Med Open 2015;2:23. https://doi.org/10.1186/s40798-016-0047-y.
[17] Friedmann B, Weller E, Mairbaurl H, Bartsch P. Effects of iron repletion on blood volume and performance capacity in young athletes. Med Sci Sports Exerc 2001;33(5):741–6. https://doi.org/10.1097/00005768-200105000-00010.
[18] Rubeor A, Goojha C, Manning J, White J. Does iron supplementation improve performance in iron-deficient nonanemic athletes? Sports Health 2018;10(5):400–5. https://doi.org/10.1177/1941738118777488.
[19] Clénin G, Cordes M, Huber A, Schumacher YO, Noack P, Noack J, et al. Iron deficiency in sports—definition, influence on performance and therapy. Swiss Med Wkly 2015;145:w14196. https://doi.org/10.4414/smw.2015.14196.
[20] Keller K, Hartung K, Del Castillo Carillo L, Treiber J, Stock F, Schröder C, et al. Exercise hypertension in athletes. J Clin Med 2022;11(16):4870. https://doi.org/10.3390/jcm11164870.
[21] Fletcher GF, Ades PA, Kligfield P, Arena R, Balady GJ, Bittner VA, et al. Exercise standards for testing and training: a scientific statement from the American Heart Association. Circulation 2013;128(8):873–934. https://doi.org/10.1161/CIR.0b013e31829b5b44.
[22] Pelliccia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, et al. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. Eur Heart J 2021;42(1):17–96. https://doi.org/10.1093/eurheartj/ehaa605.
[23] Writing C, Gluckman TJ, Bhave NM, Allen LA, Chung EH, Spatz ES, et al. 2022 ACC expert consensus decision pathway on cardiovascular sequelae of COVID-19 in adults: myocarditis and other myocardial involvement, post-acute sequelae of SARS-CoV-2 infection, and return to play: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2022;79(17):1717–56. https://doi.org/10.1016/j.jacc.2022.02.003.
[24] Steinacker JM, Schellenberg J, Bloch W, Deibert P, Friedmann-Bette B, Grim C, et al. Recommendations for return-to-sport after COVID-19: expert consensus. Dtsch Z Sportmed 2022;73(4):127–36. https://doi.org/10.5960/dzsm.2022.532.
[25] Fletcher A, Forbes A, Svenson N, Wayne Thomas D, Paper ABSfHGP. Guideline for the laboratory diagnosis of iron deficiency in adults (excluding pregnancy) and children. Br J Haematol 2022;196(3):523–9. https://doi.org/10.1111/bjh.17900.
[26] Snook J, Bhala N, Beales ILP, Cannings D, Kightley C, Logan RP, et al. British Society of Gastroenterology guidelines for the management of iron deficiency anaemia in adults. Gut 2021;70(11):2030–51. https://doi.org/10.1136/gutjnl-2021-325210.
[27] Ko CW, Siddique SM, Patel A, Harris A, Sultan S, Altayar O, et al. AGA Clinical practice guidelines on the gastrointestinal evaluation of iron deficiency anemia. Gastroenterology 2020;159(3):1085–94. https://doi.org/10.1053/j.gastro.2020.06.046.
[28] Sonoda K. Iron deficiency anemia: guidelines from the American Gastroenterological Association. Am Fam Physician 2021;104(2):211–2 https://www.ncbi.nlm.nih.gov/pubmed/34383429.
[29] DellaValle DM, Haas JD. Iron supplementation improves energetic efficiency in iron-depleted female rowers. Med Sci Sports Exerc 2014;46(6):1204–15. https://doi.org/10.1249/MSS.0000000000000208.
[30] Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28(1):1–39.e14. https://doi.org/10.1016/j.echo.2014.10.003.
[31] Sandstrom G, Borjesson M, Rodjer S. Iron deficiency in adolescent female athletes—is iron status affected by regular sporting activity? Clin J Sport Med 2012;22(6):495–500. https://doi.org/10.1097/JSM.0b013e3182639522.
[32] Roy R, Kuck M, Radziwolek L, Kerling A. Iron deficiency in adolescent and young adult german athletes—a retrospective study. Nutrients 2022;14(21):4511. https://doi.org/10.3390/nu14214511.
[33] Levi M, Rosselli M, Simonetti M, Brignoli O, Masotti M, Spatz A, et al. Epidemiology of iron deficiency anaemia in four European countries: a population-based study in primary care. Eur J Haematol 2016;97(6):583–93. https://doi.org/10.1111/ejh.12776.
[34] Mani A, Singh T, Calton R, Chacko B, Cherian B. Cardiovascular response in anemia. Indian J Pediatr 2005;72(4):297–300. https://doi.org/10.1007/BF02724008.
[35] Bunn HF. Oxygen delivery in the treatment of anemia. N Engl J Med 2022;387(25):2362–5. https://doi.org/10.1056/NEJMra2212266.
[36] Tsai KZ, Lai SW, Hsieh CJ, Lin CS, Lin YP, Tsai SC, et al. Association between mild anemia and physical fitness in a military male cohort: the CHIEF study. Sci Rep 2019;9(1):11165. https://doi.org/10.1038/s41598-019-47625-3.
[37] Dellavalle DM, Haas JD. Iron status is associated with endurance performance and training in female rowers. Med Sci Sports Exerc 2012;44(8):1552–9. https://doi.org/10.1249/MSS.0b013e3182517ceb.

[38] Pate RR, Miller BJ, Davis JM, Slentz CA, Klingshirn LA. Iron status of female runners. Int J Sport Nutr 1993;3(2):222–31. https://doi.org/10.1123/ijsn.3.2.222.

[39] McLane JA, Fell RD, McKay RH, Winder WW, Brown EB, Holloszy JO. Physiological and biochemical effects of iron deficiency on rat skeletal muscle. Am J Physiol 1981;241(1):C47–54. https://doi.org/10.1152/ajpcell.1981.241.1.C47.

[40] Celsing F, Blomstrand E, Werner B, Pihlstedt P, Ekblom B. Effects of iron deficiency on endurance and muscle enzyme activity in man. Med Sci Sports Exerc 1986;18(2):156–61 https://www.ncbi.nlm.nih.gov/pubmed/3702642.

[41] Sim M, Garvican-Lewis LA, Cox GR, Govus A, McKay AKA, Stellingwerff T, et al. Iron considerations for the athlete: a narrative review. Eur J Appl Physiol 2019;119(7):1463–78. https://doi.org/10.1007/s00421-019-04157-y.

[42] Gregg SG, Willis WT, Brooks GA. Interactive effects of anemia and muscle oxidative capacity on exercise endurance. J Appl Physiol (1985) 1989;67(2):765–70. https://doi.org/10.1152/jappl.1989.67.2.765.

[43] Davies KJ, Donovan CM, Refino CJ, Brooks GA, Packer L, Dallman PR. Distinguishing effects of anemia and muscle iron deficiency on exercise bioenergetics in the rat. Am J Physiol 1984;246(6 Pt 1):E535–43. https://doi.org/10.1152/ajpendo.1984.246.6.E535.

[44] Ohira Y, Gill SL. Effects of dietary iron deficiency on muscle fiber characteristics and whole-body distribution of hemoglobin in mice. J Nutr 1983;113(9):1811–8. https://doi.org/10.1093/jn/113.9.1811.

[45] Whiting SJ, Barabash WA. Dietary reference intakes for the micronutrients: considerations for physical activity. Appl Physiol Nutr Metab 2006;31(1):80–5. https://doi.org/10.1139/h05-021.

[46] Uijterschout L, Vloemans J, Vos R, Teunisse PP, Hudig C, Bubbers S, et al. Prevalence and risk factors of iron deficiency in healthy young children in the southwestern Netherlands. J Pediatr Gastroenterol Nutr 2014;58(2):193–8. https://doi.org/10.1097/MPG.0000000000000216.

[47] Keller K, Sagoschen I, Schmitt VH, Sivanathan V, Espinola-Klein C, Lavie CJ, et al. Obesity and its impact on adverse in-hospital outcomes in hospitalized patients with COVID-19. Front Endocrinol (Lausanne) 2022;13:876028. https://doi.org/10.3389/fendo.2022.876028.

[48] Keller K, Hobohm L, Ebner M, Kresoja KP, Münzel T, Konstantinides SV, et al. Trends in thrombolytic treatment and outcomes of acute pulmonary embolism in Germany. Eur Heart J 2020;41(4):522–9. https://doi.org/10.1093/eurheartj/ehz236.