BMJ Open Sport & Exercise Medicine

Bone health in Norwegian female elite runners: a cross-sectional, controlled study

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To cite: Kyte KH, Haakstad LAH, Hisdal J, *et al*. Bone health in Norwegian female elite runners: a cross-sectional, controlled study. *BMJ Open Sport & Exercise Medicine* 2023;**9**:e001472. doi:10.1136/bmjsem-2022-001472

Accepted 8 February 2023

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ABSTRACT

Objective The primary objective was to compare bone mineral density (BMD) in Norwegian female elite long-distance runners with a control group of inactive females. Secondary objectives were to identify cases of low BMD, to compare the concentration of bone turnover markers, vitamin D and symptoms of low energy availability (LEA) between the groups, and to identify possible associations between BMD and selected variables.

Methods Fifteen runners and fifteen controls were included. Assessments included dual-energy X-ray absorptiometry measurement of BMD in the total body, lumbar spine and dual proximal femur. Blood samples included endocrine analyses and circulating bone turnover markers. The risk of LEA was assessed through a questionnaire.

Results Runners had higher Z-scores in the dual proximal femur (1.30 (0.20 to 1.80) vs 0.20 (−0.20 to 0.80), p<0.021) and total body (1.70 (1.20 to 2.30) vs 0.90 (0.80 to 1.00), p<0.001). The lumbar spine Z-score was similar between groups (0.10 (−0.70 to 0.60) vs −0.10(−0.50 to 0.50), p=0.983). Three runners had low BMD (Z-score <−1) in the lumbar spine. Vitamin D and bone turnover markers showed no differences between the groups. Forty-seven per cent of the runners were at risk of LEA. Dual proximal femur BMD showed a positive correlation to estradiol and a negative correlation to LEA symptoms in runners.

Conclusion Norwegian female elite runners had higher BMD Z-score in the dual proximal femur and total body compared with controls, while no difference was observed in the lumbar spine. The advantages of long-distance running on bone health seem to be site specific, and there is still a need for the prevention of LEA and menstrual disorders in this group.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Weight-bearing physical activity benefits the skeleton.
⇒ Long-distance runners are at risk for low energy availability (LEA), an important risk factor for low bone mineral density (BMD).

WHAT THIS STUDY ADDS

⇒ Norwegian female elite runners have higher total body BMD and dual proximal femur BMD than age-matched inactive controls.
⇒ The advantages of long-distance running on the skeleton seem to be site specific.
⇒ Twenty per cent of the runners were classified with low BMD in the lumbar spine, and 47% were at risk for LEA.
⇒ Female elite runners may be at risk for LEA despite having normal BMD (Z-score ≥1).

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ There is still a need to prevent LEA and menstrual disorders among female elite long-distance runners to ensure these women reach their potential for a healthy skeleton.
⇒ Our finding raises the issue of site-specific screening for low BMD in this population, possibly with sports-specific cut-off ranges for BMD Z-scores adapted to runners.

INTRODUCTION

Physical activity and exercise influence bone mineral density (BMD) and contribute to a healthy skeleton.[1] During its impact on the remodelling process, weight-bearing exercise may play a central role in achieving optimal bone health in athletes.[2 3] In addition, optimal energy availability and endocrine state are essential factors in achieving a healthy skeleton.[4] However, excessive exercise stress combined with a restrictive energy intake may result in low energy availability (LEA), disturbed hormonal levels, reduced body fat and increased bone stress injuries.[5]

In weight-dependent sports, like long-distance running, the impact on BMD is multifaceted. This is mainly due to LEA, which threatens the initial positive effect of weight-bearing activities on BMD. Further, estradiol plays a key role in regulating the balance between bone resorption and formation. In addition, LEA has been linked to suboptimal vitamin D and calcium status, which is essential to achieve a healthy skeleton.[1 3 6]

The complexity of factors that affect bone health in athletes has also called into question

whether the current cut-off values are appropriate to use when assessing BMD in athletes. In athletes, a Z-score ≥−1.0 is defined as normal, according to the American College of Sports Medicine and the International Olympic Committee.[6 7] It has recently been suggested by The International Society For Clinical Densitometry[8] and Jonvik *et al*[9] that a sport/event-specific Z-score range is needed to initiate early treatment for high-risk athletes. This will require increased knowledge about BMD in athletes in various sports, and this study will contribute to further knowledge about BMD in female elite Caucasian runners.

Low BMD has earlier been observed in long-distance runners, despite competing in a weight-bearing sport.[10–14] Most studies have focused on elite adolescent runners[12 13] or adult runners below the elite level.[11] Barrack *et al*[12] observed low BMD (Z-score <−1) in 39.8% of female adolescent runners. Rauh *et al*[13] observed low BMD (Z-score <−1) in 35.9% of female high school runners. Adolescent runners with low BMD may struggle with this in adulthood as well.[15] On the other hand, low BMD may be partially reversible before age 30.[16] Hence, we cannot necessarily transfer the results from adolescent to adult runners.

There is limited research on BMD among adult elite Caucasian runners. Preventive strategies and screening are of utmost importance as elite athletes represent a population at elevated risk for overuse injuries and diseases, including bone stress injuries. Hence, it is important to acquire further knowledge about bone health in this population. Based on previous studies on female adolescent runners and runners below the elite level, we hypothesised that female elite long-distance runners have lower BMD than inactive controls.

The primary objective of this study was to compare BMD in the total body, lumbar spine and dual proximal femur in female elite long-distance runners with a control group of inactive females. Secondary objectives were to identify cases of low BMD, to compare the concentration of bone turnover markers, vitamin D and symptoms of LEA between the groups, and to identify possible associations between BMD and endocrine state, symptoms of LEA and anthropometric parameters.

METHODS

Study design and recruitment

The present cross-sectional study is part of a larger study of the same population. The main aim was to investigate vascular function in Norwegian female elite long-distance runners.[17] Overlap includes age, height, weight, training data, fat mass, hormone levels and the LEA in Female Questionnaire (LEAF-Q). Power analysis was done for the main outcome, endothelial function, in the overall study on vascular function. However, in addition, post hoc power analysis has been performed for the primary objective of the current study and presented in the results section. Written information about the study was distributed to female runners in the top 20 long-distance running statistics lists in Norway in 2019 and announcements on social media. Recruitment focused on long-distance running (footraces ranging from 5 km to half-marathon), including trail running. According to the recently published paper from McKay *et al*,[18] 10 runners qualified as 'elite' by competing at the international level (including track, road and trail running), and 5 runners competed at the national level, representing 'highly trained' runners.[18] The whole runners' group will be referred to as 'elite runners' hereafter. A control group of physically inactive women was recruited among students at the University of Oslo. The inclusion criteria were age 18–35 years, healthy, non-smoking and nullipara. Training criteria were a minimum of 8-hour endurance training weekly for the runners and a maximum of 2-hour training weekly for the controls. Sixteen runners and 17 physically inactive women were recruited between October 2019 and January 2020. All participants signed written informed consent. One runner and two controls were withdrawn from the study due to injury or challenges during the COVID situation. The final analysis included 15 runners and 15 controls. Both study groups were Caucasian.

The study was conducted during three different test days. The overall study[17] included vascular function tests, performed on the first test day. In addition, the participants answered the LEAF-Q.[19] At the second visit, all blood samples were collected. The BMD and maximal oxygen consumption (VO_{2max}) were measured at the third visit.

Measurements

The primary outcome, BMD (gCal/cm^2) and body composition were measured by DXA (Lunar, Prodigy Densitometry, GE Medical Systems, USA). DXA measurements included the lumbar spine (L1–L4), dual proximal femur and total body. Low BMD was classified as having a Z-score of <−1 for a minimum one of the measured sites. Height and body weight were measured before the DXA scan.

The LEAF-Q, a validated questionnaire regarding symptoms of LEA, was answered by all participants. A total score of ≥8 is normally considered at risk of LEA.[19] Amenorrhoea was defined as no bleeding for the last 3 months, based on self-reporting through the LEAF-Q.

Blood samples were collected from a peripheral vein in a resting state between 08:00 and 10:00 hours after an overnight fast and before exercise. Sample collection, performed during the menstrual cycle days 1–7, included hormone analyses (estradiol, luteinising hormone (LH), follicle-stimulating hormone (FSH), testosterone, sex hormone-binding globulin (SHBG), thyroid-stimulating hormone (TSH) and free thyroxine (fT4), 25-OH Vitamin D (total) and circulating bone turnover markers (N-terminal propeptide of type 1 procollagen (PINP) and C-terminal telopeptide of type 1 collagen (CTX-1)).

Blood analyses were performed at the Hormone Laboratory, Oslo University Hospital. TSH was measured

with non-competitive immunofluorometric analysis by Autodelfia (Wallac Oy, Turku, Finland), and fT4 was measured with solid-phase time-delayed fluoro-immunoassay with back-titration by Autodelfia (Wallac Oy, Turku, Finland). Estradiol was determined using chemiluminescence immunoassay. FSH, LH and SHBG were determined using a non-competitive immunolumi-nometric assay. Testosterone and 25-OH vitamin D were determined using liquid chromatography-tandem mass spectrometry. PINP and CTX-1 were determined using electrochemiluminescence immunoassay. Analytical coefficients of variation: TSH, 3%, fT4, 5%, estradiol, 11%, FSH, 7%, LH, 9%, SHBG, 7%, testosterone, 12%, 25-OH vitamin D, 11%, PINP, 5%, CTX-1, 6%.

VO_{2max} was conducted using a breath-by-breath gas analysis system (OxyconPro analyzer; Jaeger, Würtzburg, Germany) on a treadmill (ELG 90/200 Sports; Woodway, Weil am Rhein, Germany) with increasing speed every minute until exhaustion.

Statistical analysis

Statistical analyses were performed in SigmaPlot V.14.0 (Systat Software, San Jose, California, USA). The normality test (Shapiro-Wiik) failed for some of the variables, and we used the median (25–75th percentile) throughout. Non-parametric statistics (Mann-Whitney rank sum test) were used to test for significant differences between the groups. Pearson's correlation coefficient was used to explore associations between selected variables. A value of p<0.05 was accepted as statistically significant.

RESULTS

Participants' characteristics are presented in table 1. Runners' median and mean weekly running distances were 120 km (110–120) and 118 km (±19). Seven of the runners (47%) were classified at risk of LEA, with a total LEAF-Q score ≥8 (19). Two controls (13%) had a LEAF-Q score ≥8. Three runners (20%) and none of the controls reported having amenorrhoea at the time. All these three runners were classified at risk of LEA, and two had low BMD (Z-score <−1) in the lumbar spine. In addition, three runners (20%) reported a history of amenorrhoea in the past. One of these was classified at risk of LEA and had low BMD (Z-score <−1) in the lumbar spine.

Bone health

Bone health data are presented in table 2. BMD Z-score for different measuring points is shown in figure 1. Runners had significantly higher Z-scores in the dual proximal femur (p=0.021) and total body (p<0.001), while the lumbar spine Z-score was similar between groups. Low BMD was observed in three runners (20%), all in the lumbar spine. These runners had a history of amenorrhoea, two at present and one in the past, and had a LEAF-Q score ≥8. No controls had low BMD. There were no participants with Z-score <-2.

Endocrine data and bone health

Runners showed significantly lower levels of estradiol (0.08 nmol/L) and LH (2.00 IU/L) than controls (0.23 nmol/L and 5.10 IU/L) p=0.033 and p=0.003, respectively. FSH, testosterone, SHBG, TSH and fT4 were not different between groups.

In runners, a significant positive correlation between estradiol and dual proximal femur BMD was observed (r=0.664, p=0.013), while there was no significant association to the lumbar spine or total body BMD. Symptoms of LEA showed a significant negative correlation to dual

Table 1 Participants' characteristics, health and fitness status in runners and controls

	Runners (n=15)	Controls (n=15)	P value
Age (year)	27.0 (25.0–30.0)	26.0 (24.0–28.0)	0.390
Height (cm)	169.5 (164.0–178.0)	173.0 (168.0–178.0)	0.349
Weight (kg)	55.8 (54.0–61.4)	64.5 (62.0–72.5)	<0.001*
BMI (kg/m^2)	19.7 (19.1–21.2)	22.0 (20.7–24.5)	<0.001*
Fat mass (%)	17.0 (16.2–19.4)	30.4 (25.2–33.9)	<0.001*
Fat mass (g)	9134 (8163–10859)	19 041 (15 939–22599)	<0.001*
Fat-free mass (g)	46 849 (46 011–51502)	48 167 (43 952–49672)	0.678
Fat-free mass (%)	84.7 (82.7–85.3)	71.5 (67.8–76.5)	<0.001*
LEAF-Q (total score)	7.0 (5.0–9.0)	3.0 (1.0–5.0)	0.002*
VO_{2max} (mL/kg/min)	64.0 (62.4–66.2)†	44.7 (41.4–45.5)	<0.001*
Endurance training (hours/wk)	11.0 (9.0–15.0)	1.0 (0.0–1.0)	<0.001*
Training (hours/wk)	12.0 (11.0–15.0)	2.0 (1.0–3.5)	<0.001*

Values are expressed as median (25, 75 percentiles).
P values refer to the difference between groups.
*p<0.05.
†Missing data from one participant.
BMI, body mass index; LEAF-Q, low energy availability in females questionnaire; VO_2max, maximal oxygen consumption.;

Table 2 BMD and bone turnover parameters in runners and control group

	Runners (n=15)	Controls (n=15)	P value
BMD total body (g/cm^2)	1.212 (1.141–1.344)	1.193 (1.168–1.227)	0.229
BMD L-spine L1-L4 (g/cm^2)	1.202 (1.057–1.259)	1.193 (1.159–1.273)	0.419
BMD D.P. femur (g/cm^2)	1.139 (0.990–1.191)	1.055 (0.973–1.110)	0.074
Z-score total body	1.70 (1.20–2.30)	0.90 (0.80–1.00)	<0.001*
Z-score L-spine L1-L4	0.10 (–0.70–0.60)	–0.10 (–0.50–0.50)	0.983
Z-score D.P. femur	1.30 (0.20–1.80)	0.20 (–0.20–0.80)	0.021*
Vitamin D (nmol/L)	68.0 (59.0–83.0)	55.0 (44.0–73.0)	0.177
CTX-1 (ug/L)	0.390 (0.285–0.640)	0.560 (0.470–0.670)	0.140
P1NP (ug/L)	63.0 (46.0–94.0)	78.0 (62.0–112.0)	0.125

Values are expressed as median (25, 75 percentiles).
P values refer to the difference between groups.
*p<0.05.
BMD, bone mineral density; D.P. femur, dual proximal femur; L-spine, lumbar spine; P1NP, N-terminal propeptide of type 1 procollagen.

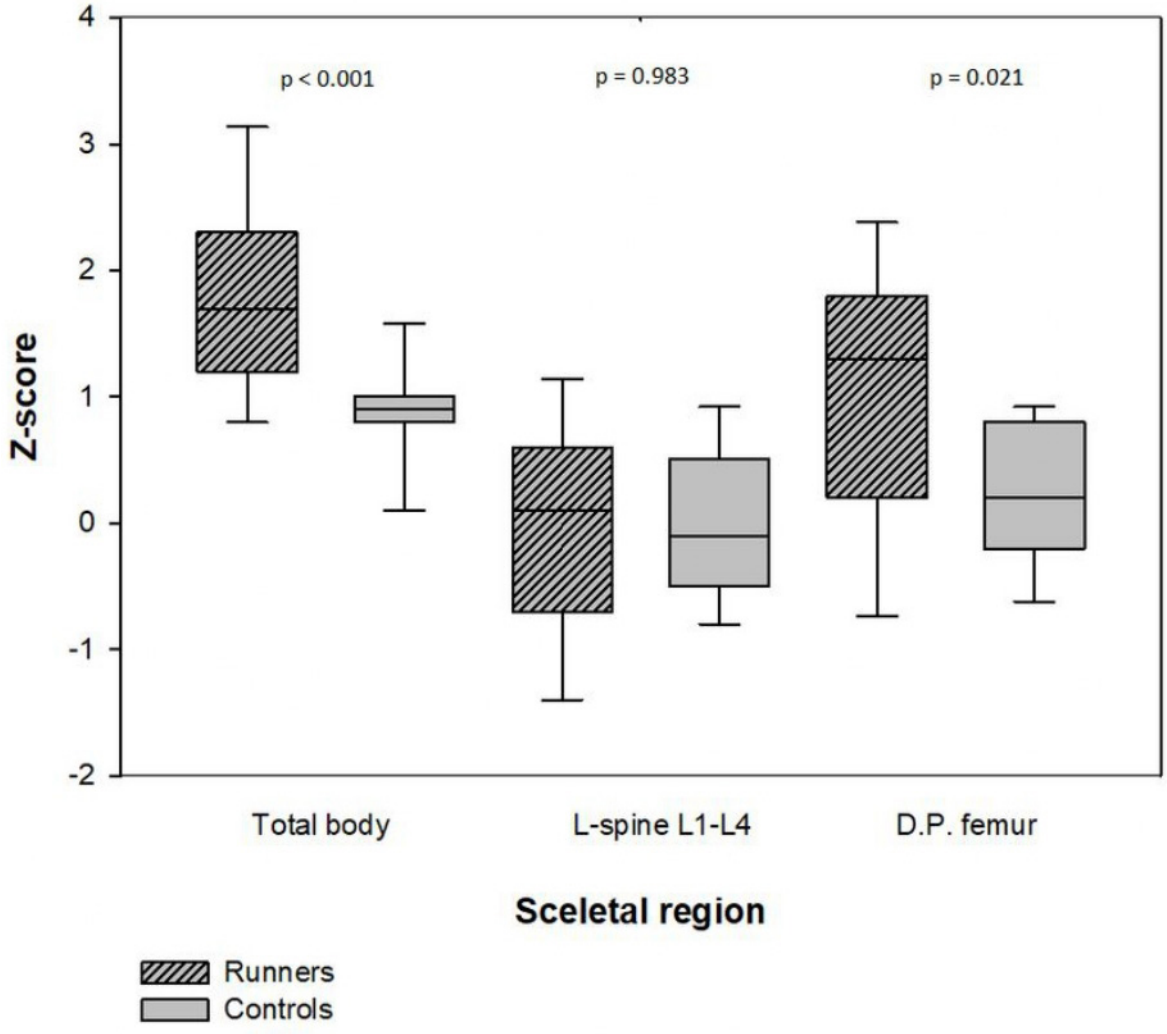

Figure 1 Bone density Z-score in runners and controls.

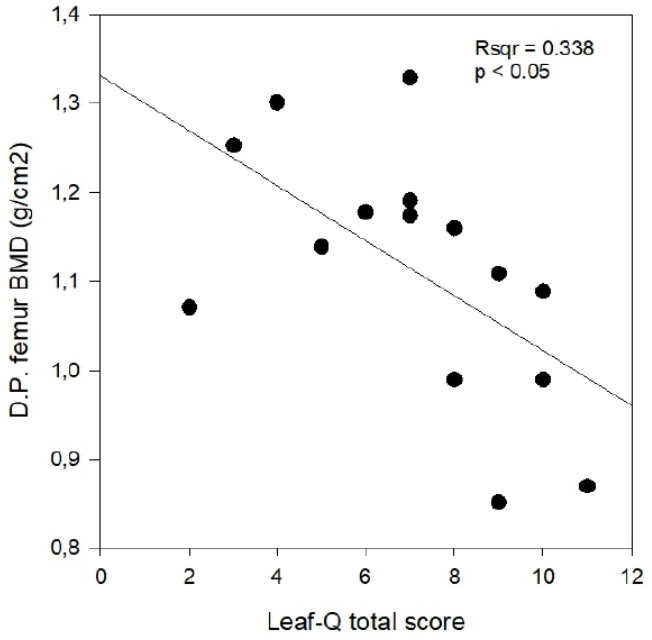

Figure 2 Leaf-Q and D.P. femur BMD in runners. BMD, bone mineral density; D.P. femur, dual proximal femur.

proximal femur BMD in runners (figure 2), with no significant association with the lumbar spine or total body BMD. Body weight was positively correlated to total body BMD and dual proximal femur BMD in runners (r=0.617, p=0.014 and r=0.525, p=0.045), while the correlation to lumbar spine BMD was borderline (r=0.503, p=0.056).

In controls, there was no association between estradiol and BMD nor between symptoms of LEA and BMD. Body weight was positively correlated to total body BMD (r=0.637, p=0.011), while there was no significant correlation to lumbar spine BMD or dual proximal femur BMD in controls.

DISCUSSION

Our main findings were that female elite long-distance runners had significantly higher BMD Z-scores in the dual proximal femur and total body compared with age-matched inactive controls. Further, the lumbar spine Z-score was comparable between groups.

Secondary findings were that we identified three runners (20%) with low BMD (Z-score <−1) in the lumbar spine. Forty-seven per cent of the runners were at risk of LEA. Dual proximal femur BMD was positively associated with estradiol and negatively associated with symptoms of LEA in runners. Vitamin D and bone turnover markers showed no differences between groups.

Site-specific differences in BMD

Our observation of higher BMD Z-score in the dual proximal femur and total body among runners compared with controls is consistent with previous studies.[20–22] Duckham *et al* observed 14% higher proximal femur BMD in eumenorrheic athletes than controls.[20] McCormack *et al* observed a higher total body BMD Z-score in collegiate runners compared with controls (0.030 vs −0.821).[22] Femurs are exposed to high mechanical loading when running, which is currently understood to positively affect BMD.[23]

Strain from running affects the spine and femur differently, where the spine is exposed to less mechanical stress than the femur and thus does not receive the same positive effect on skeletal strength.[14 22] A difference between cortical and trabecular bones' response to strain may also contribute to this difference.[24] These are possible explanations for our study's comparable lumbar spine Z-score between runners and controls.

BMD, LEA and endocrine state

The prevalence of low BMD was site specific, limited to the lumbar spine, and observed in the runners' group only. Further, the three runners with low BMD had a history of amenorrhoea. The major consequence of hypoestrogenism due to LEA is low BMD and increased fracture risk.[25] Hence, our findings support the well-known relationship between amenorrhoea and impaired bone health.[5 6] Despite energy availability was not measured in our study population, these three runners were at risk for LEA.

To prevent bone stress injuries and impaired bone health, addressing the state of LEA is crucial when identifying low BMD in athletes with menstrual disturbances.[25] In such cases, restoration of energy availability will be the preferred solution, however challenging in a sports environment where performance is a priority.[26 27]

The risk of LEA was not limited to the three runners with low BMD. Almost half of the runners (47%) presented a LEAF-Q score consistent with being at risk of LEA. Prolonged/repeated periods with LEA are the non-genetic factor most commonly causing low BMD in athletes. Hence, we should be vigilant even if an athlete shows BMD values within the reference range. Further, the range of reference values is interesting here, as the understanding of increased BMD due to mechanical loading may be important for how we should assess the BMD in athletes.[9] Jonvik *et al* have recently suggested establishing sport/event-specific cut-off ranges for BMD Z-scores.[9] This may help us not ignore important early-sign information of impaired bone health, such as the combination of the risk of LEA and a BMD just within normal values, that is, a BMD Z-score between 0 and −1. Due to the high risk of LEA among runners,[5] it is essential not to overlook a symptom of LEA by relying on acceptable BMD values alone. That may prevent us from giving early interventions before more severe consequences such as bone stress injuries and osteoporosis occur.

According to LEAF-Q, it is important to emphasise that this is a screening tool to identify individuals at risk of LEA and cannot be used to determine whether the runners suffer from LEA.[19] Further, exogenous hormones override the natural menstrual cycle and may mask an oligomenorrheic or amenorrheic state caused by LEA. In this study, we observed lower levels of estradiol

and LH in runners compared with controls. Preservation of gonadal function depends on energy availability.[6] Menstrual disorders in athletes due to LEA range from anovulatory cycles and luteal phase defects to oligoamenorrhoea.[6 28] Hence, a tendency towards functional hypothalamic amenorrhoea in the runners group is a possible explanation for the observed differences in sex hormones between groups.[29]

Associations between BMD, endocrine state and symptoms of LEA

In this study, dual proximal femur BMD was positively associated with estradiol and negatively associated with symptoms of LEA in runners. These associations support that sufficient estradiol levels and adequate energy availability are important for optimal bone health. On the other hand, we observed no association between lumbar spine BMD and estradiol, nor between lumbar spine BMD and symptoms of LEA. This is surprising as oestrogen deficiency has been associated with low lumbar spine BMD in previous research.[30] Thus, it is possible that our study was underpowered to show this relationship.

Vitamin D and bone turnover markers

P1NP and CTX-1 showed no differences between the groups. CTX-1 and P1NP are reference biomarkers for measuring bone resorption and formation, respectively.[31] Previous research has shown that LEA suppresses bone formation markers while bone resorption markers increase.[27] Thus, our results indicate no significant difference in bone formation or resorption in this selection of runners and controls. However, biomarkers of bone metabolism are typically measured systemic and, therefore, do not necessarily reflect bone remodelling at each specific site.[32 33] Finally, satisfactory levels of vitamin D in both groups and no difference between the groups suggest that vitamin D status cannot explain the differences we observed in BMD.

Strengths and limitations

The sample consisted of a homogeneous group of highly trained females, and a control group was included. We defined the runners as 'elite' when we carried out the study. Still, according to a recently published paper by McKay *et al*,[18] the majority of the runners (n=10) qualified as 'elite', the rest (n=5) as 'highly trained' runners.[18] Thus, it is likely that our runners are representative of a larger cohort of Norwegian female elite runners. All participants were Caucasian, making our results generalisable to female elite/highly trained Caucasian runners in other countries. Even though elite runners are more challenging to recruit than recreational runners, we limited our inclusion to a homogenous group of highly trained individuals. However, possibly at the expense of a larger sample size and statistical limitations. Further strengths of this study are the use of several reliable methods, including the validated LEAF-Q, blood samples and DXA.

Limitations of this study include the cross-sectional study design, which cannot establish a causal relationship. Further, hormonal contraceptives among some participants may hide an underlying menstrual disturbance.[34] However, many elite runners use hormonal contraception,[34] and our population may be considered representative. The history of bone stress injuries and information about energy intake and sports participation in childhood and adolescence could be interesting but were not collected.

Practical implications

Although the runners in our study had higher BMD in the femur and total body than controls, we identified runners with low lumbar spine BMD (Z-score <−1). Further, elite runners may be at risk for LEA despite having normal BMD values. Questions have been raised about whether the BMD reference values are suitable for athletes. Elite athletes may represent a population at elevated risk for bone stress injuries. Hence preventive strategies and site-specific screening for all runners who show signs of LEA should be considered. Signs of LEA must not be limited to amenorrhoea, as hormonal contraception can mask this.

CONCLUSION

Norwegian female elite runners had higher BMD Z-scores in the dual proximal femur and total body compared with inactive controls, while no difference was observed in the lumbar spine. Further, dual proximal femur BMD showed a positive correlation to estradiol and a negative correlation to symptoms of LEA in runners. These correlations were not present in the control group. According to this study, the advantages of long-distance running on bone health seem to be site specific, further supported by the fact that cases of low BMD were restricted to the lumbar spine among runners with a history of amenorrhoea. There is still a need for the prevention of LEA and menstrual disorders in this group.

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Acknowledgements The authors would like to thank the participants for their commitment to this study.

Contributors KHK, JH and TS conceived and designed the study. KHK and AS carried out the data collection and processing. KHK and JH performed the data analysis. All authors contributed to the data interpretation. KHK drafted the original manuscript. KHK, JH, TS and LAHH reviewed and edited the manuscript. Supervision: JH, TS and LAHH. All authors approved the final manuscript. KHK is the study guarantor.

Funding The study was financially supported by The Research Council of Norway through the Medical Student Research Program at the University of Oslo, specified to the first author.

Disclaimer The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The study was approved by the Regional Committees for Medical and Health Research Ethics (REC South East, reference 2019/155). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data set is available from the corresponding author on reasonable request.

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