

The female athlete triad

Amanda Weiss Kelly, Suzanne Hecht

University Hospitals of Cleveland, Rainbow Babies and Children's Hospital, Case Western Reserve University, Cleveland, OH, USA

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Correspondence to: Amanda Weiss Kelly, MD. University Hospitals of Cleveland, Rainbow Babies and Children's Hospital, Case Western Reserve University, Cleveland, OH, USA. Email: Amanda.weiss@uhhospitals.org.

Abstract: The female athlete triad represents the 3 interrelated components: of energy availability (EA), menstrual function and bone health. Each component exists on a spectrum ranging from optimal health to dysfunction. Screening for the triad during the annual wellness exam, the preparticipation physical evaluation (PPE) or when the athlete presents with any single component can help identify athletes at risk. A multidisciplinary team is helpful in managing the treatment of the Triad which relies on improving EA. Screening, early recognition and aggressive treatment is important, especially in adolescent athletes to optimize bone health.

Keywords: Bone density; energy intake (EI); amenorrhea; female athlete triad syndrome/diagnosis; female athlete triad syndrome/therapy; exercise

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The female athlete triad was first recognized in the 1990s as a disorder of 3 interrelated components, amenorrhea, osteoporosis and disordered eating that affected physically active females (1,2). Over time, it has been recognized that each element of the triad exists on a continuum from optimal health to disease. And, the 3 components are now termed menstrual function, bone mineral density (BMD), and energy availability (EA). The spectrum for menstrual function ranges from eumenorrhea to functional hypothalamic amenorrhea (FHA), for bone health from optimal bone health to osteoporosis and for EA from optimal EA to low EA +/- eating disorder (ED). This more inclusive definition more accurately represents the triad diagnosis. Both EA and menstrual function directly affect bone health and EA directly influences menstrual function (3). Athletes may present with a single component or any combination of the 3 components and may be anywhere along the spectrum of each component (4).

The complexity of evaluation of each of the components of the triad makes it difficult to determine the true prevalence of the triad. The prevalence of female athletes

exhibiting one component of the triad ranges from 16–54% and ranges from 0–16% for athletes exhibiting all 3 components (5). Athletes participating in aesthetic sports, weight class sports, sports that emphasize leanness and endurance sports are at increased risk for developing triad related conditions but athletes in any sport can be affected (3).

EA

EA refers to the dietary energy left over for all other physiologic functions after daily exercise energy expenditure (EEE) is accounted for and is defined as daily dietary energy intake (EI) minus daily EEE (kcal)/fat free mass FFM (kg) (2,3). An EA of 45 kcal/kg FFM per day in adult females has been recognized as optimal EA (3). In growing adolescents, optimal EA has not been well defined, and may be higher than in adults (4). EA below 30 kcal/kg FFM per day has associated with menstrual disturbances and disruptions in bone mineralization (6,7). Data does suggest that this is not an absolute threshold and that individual variability

Table 1 ISCD clinically significant fracture (23)

2 or more long bone fractures by age 10
3 or more long bone fractures at any age up to age 19
ISCD, International Society for Clinical Densitometry.

exists with some athletes experiencing disruptions in physiologic function at higher or lower levels of EA (6,8). It is important to recognize that stable body weight does not necessarily reflect adequate EA (3). Amenorrheic athletes may achieve energy balance, and stabilization of weight, via physiological mechanisms that alter metabolic rate, growth and reproduction (3).

While some athletes with low EA meet DSM-V criteria for ED, exhibit disordered eating behaviors or use pathological weight control techniques, many female athletes with inadequate EA do not intentionally restrict calories and do not exhibit disordered eating (DE)/ED behaviors (9). Others may restrict calories intentionally to achieve athletic goals, without meeting criteria for DE/ED. Dieting, injury, coaching changes and comments from family member, friends and coaches have been identified as potential risk factors for the development of DE behaviors in athletes (10).

A dose-response relationship between restrictions in EA and suppression of estradiol, increased bone resorption and decreased bone formation has been observed (6). And, low EA is associated with decreased BMD even in the absence of menstrual dysfunction (3).

Decreased EA may also have a negative effect on sports performance, as demonstrated by decreased performance in junior elite swimmers with energy deficiency and menstrual dysfunction compared to eumenorrheic swimmers (11).

Due to the difficulty in measuring EA, little data exists regarding the prevalence of low EA in athletes, one study found that 36% of athletes had EA \leq 45 kcal/kg FFM (12). The prevalence of DE/ED ranges from 0–60% (5).

Menstrual function

Menstrual dysfunction is common in female athletes and the prevalence ranges from 1–64% (5,8,12,13).

Alterations in menstrual function seen in the triad include anovulation, luteal phase dysfunction, oligomenorrhea (infrequent cycles $>$ 35 days in length), secondary amenorrhea (cessation of menstrual periods for \geq 3 consecutive months) and primary amenorrhea

(absence of menses by age 15). Anovulation and luteal phase dysfunction can be difficult to diagnose since menstrual cycles may continue at regular intervals. The menstrual dysfunction in the triad is hypothalamic in origin and is termed functional hypothalamic amenorrhea (FHA). Low EA leads to alterations in GnRH pulsatility causing decreased LH pulse frequency and amplitude (2,3). Disruptions in LH pulsatility have been noted within 5 days of reduced EA below 30 kcal/kg FFM (14,15).

A dose response relationship between the magnitude of energy deficiency and frequency of menstrual disturbances has also been documented (16).

Menstrual dysfunction is directly associated with lower BMD in athletes. Amenorrheic and oligomenorrheic athletes have lower BMD than their eumenorrheic counterparts (5,9,17) and are significantly more likely to sustain bone stress injury (2,17,18). And, the duration of amenorrhea in adolescent athletes is an independent predictor of lower bone density (9). Furthermore, college-aged runners with menstrual dysfunction experience more severe stress fractures than their eumenorrheic counterparts (19). In addition to impairments in BMD, menstrual dysfunction has been associated with unfavorable changes in bone microarchitecture and geometry (20-22).

Bone health

The International Society for Clinical Densitometry (ISCD) has published guidelines for evaluating BMD in premenopausal women and children (23). In these populations, the ISCD recommends that BMD be expressed as Z-scores which compares individuals to age and sex-matched controls. In premenopausal women, a Z-score of -2.0 or lower is defined as “below the expected range for age”. In children and adolescents, the ISCD preferred sites for assessment of BMD are the PA spine and total body less head (TBLH). In children, the ISCD recommends the use of the term “low bone mineral density” when BMD Z-scores are less than or equal to -2.0 and that the term osteoporosis only be used when there is a history of vertebral compression fracture or a history of clinically significant fracture in addition to low BMD (*Table 1*). Because athletes who participate in weight bearing sports typically have higher BMD than non-athletes, the American College of Sports Medicine (ACSM) recommends further evaluation for secondary causes of low BMD in athletes with BMD Z-scores less than -1.0 , even when a history of fracture is not present. The ACSM recommends the use of the term

“low BMD” in athletes with BMD Z-scores between -1.0 and -2.0 who also have a history of nutritional deficiencies, hypoestrogenism, or stress fracture (3). The ACSM defines “osteoporosis” as athletes with BMD Z-scores less than or equal to -2.0 and a history of nutritional deficiencies, hypoestrogenism, or stress fracture (3). Risk factors for low BMD in female athletes include older age at menarche, oligo- or amenorrhea, increased dietary restraint, longer period of time in endurance sports and lower BMI (4).

Though weight bearing exercise has been associated with improved BMD, a growing body of research demonstrates that impaired bone health is common in endurance athletes. As many as 41–45% of elite endurance athletes have low BMD (8,13,17,22). High-impact (e.g., gymnastics, volleyball) and odd-impact training (e.g., soccer, racquet sports) appear to have more positive effects on BMD than endurance training (22). Participation in high- and odd-impact sports during early puberty is associated with higher peak BMD, and continued sports participation beyond puberty helps to maintain these BMD gains (22). The maximal rate of bone formation typically occurs from ages 10–14 years and peak bone mass is usually attained between 20–30 years of age (24,25). Thus, it is particularly important to recognize and intervene immediately when triad disorders are identified in young athletes because childhood and adolescence are critical time periods for bone development.

Both decreased EA and low estrogen levels independently contribute to decreased BMD in female athletes (15). Markers for both bone formation and resorption are reduced in amenorrheic athletes, indicating overall decreased bone turnover (4,9). Lower estradiol levels are associated with both increased bone resorption and decreased bone formation (6).

Cardiovascular function

Unfavorable lipid profiles and impaired endothelial function have been documented in athletes with menstrual dysfunction. Flow-mediated dilation (FMD) has been used to assess endothelial function in athletes and decreased FMD has been demonstrated in amenorrheic athletes participating in endurance and non-endurance sports compared to eumenorrheic athlete and non-athlete controls (20). However, the long term cardiovascular outcomes in athletes affected by the triad have not been determined.

Male athletes

There is a small, but growing body of evidence that suggests that male athletes with low EA may experience hormonal changes, lower BMD and increased injury risk. Male athletes participating in endurance sports have lower BMD, per cent expected weight and BMI compared to those participating in power or ball sports (26,27). Low body weight and higher weekly running mileage have been identified as significant risk factors for lower BMD in male athletes (26). Several cross-sectional studies have found that male athletes involved in endurance sports such as cycling and running may have an increased risk of inadequate calorie intake and lower levels of reproductive hormones (22). Adolescent males with anorexia nervosa have lower BMD in the spine, hip, femoral neck and whole body compared to controls (28).

Screening

In high school aged athletes, screening for the triad disorders can occur during the annual well-child visit and/or the preparticipation physical evaluation (PPE) (Supplementary). In college, or older athletes screening should occur at the time of the PPE. The Female Athlete Triad Coalition has developed a 12-question screening tool (Table 2) (2). The fourth-edition PPE monograph, endorsed by 6 US medical societies, contains 8 of the 12 questions recommended by the Female Athlete Triad Coalition. Additionally, if an athlete presents for evaluation of one component of the triad, further evaluation to determine the presence of the other components should occur.

The Female Athlete Triad Coalition Consensus Statement (2) in 2014 recommends an additional tool that can be used at the time of the PPE to determine cumulative risk for poor outcomes related to the triad and recommends levels of clearance based on risk stratification with the total number of points accumulated using the tool. Each of the triad risk factors; EA, menstrual status and bone density, is assessed and assigned a point value based on severity.

In the tool, each of the following items represents moderate risk and is assigned a point value of one.

- ❖ Some dietary restriction, current DE or history of DE;
- ❖ BMI between 17.5–18.5 or <90% expected weight or weight loss 5–10% in a month’s time;
- ❖ Menarche age 15–16 years of age;

Table 2 Female athlete triad coalition consensus screening questions (2)

Have you ever had a menstrual period?
How old were you when you had your first menstrual period?
When was your last menstrual period?
How many periods have you had in the past 12 months?
Are you currently taking any female hormones (estrogen, progesterone, birth control pills)?
Do you worry about your weight?
Are you trying to or has anyone recommended that you gain or lose weight?
Are you on a special diet or do you avoid certain types of foods or food groups?
Have you ever had an eating disorder?
Have you ever had a stress fracture?
Have you ever been told that you have low bone density, osteopenia or osteoporosis?

Table 3 Causes of secondary amenorrhea in athletes (4)

Pregnancy
Polycystic ovarian syndrome
Pituitary tumor
Prolactinoma
Thyroid disorders
Liver/kidney disease
Medications: oral contraceptive pills, chemotherapy, antidepressants, antipsychotics, corticosteroids
Cushing syndrome
Malabsorption syndromes

- ❖ Oligomenorrhea 6–9 menses in 12-month period;
- ❖ History of 1 stress fracture.

Each of the following items represents high risk in the tool and is assigned a value of 2 points:

- ❖ Meets DSM-V criteria for ED;
- ❖ BMI ≤ 17.5 or $< 85\%$ expected weight;
- ❖ Menarche ≥ 16 years of age;
- ❖ < 6 menses in 12-month period;
- ❖ ≥ 2 stress fracture or ≥ 1 high risk stress fracture or trabecular bone stress injury.

Athletes who accumulate 0–1 points are considered to be at low risk for experiencing triad related complications

and do not require intervention. Athletes who score in the range of 2–5 points are considered to be at moderate risk and it is recommended that they either be cleared for full participation with close follow to ensure that all recommendations are being followed or receive limited clearance for participation with decreased training or competition schedule, to be increased as health status improves. Athletes with ≥ 6 points are considered to be at high risk and may be provisionally restricted from participation or disqualified. Data directly correlates higher scores on this risk assessment tool with increased risk for bone stress injury (29,30).

Diagnosis and evaluation

The first step in the diagnosis of the triad is a complete history that assesses daily nutritional intake, exercise habits and menstrual function. Menstrual history should include age at first menses and current or prior history of oligo-/amenorrhea and number of menses in the last 12 months. A thorough physical exam should evaluate for low BMI, orthostatic hypotension, bradycardia and signs of ED including lanugo, hypocarotenemia, parotid gland swelling, callus on the proximal interphalangeal joint and cold/discolored hands or feet. Physical exam is often normal in athletes with the triad, particularly when low EA is inadvertent.

Low BMI ($< 17.5 \text{ kg/m}^2$) or body weight $< 85\%$ of expected body weight (expected body weight is 50% for height) in adolescents may indicate low EA and has been associated with lower BMD (9). Accurately measuring EA can be difficult as methods for determining EE, dietary intake and FFM are often imprecise. Wearable technology has improved the ability to assess EE (31). Estimation of EI can be achieved with 3-, 4- and 7-day logs, 24 h dietary recall and food frequency questionnaires, but accurate measurement is challenging as inaccurate recall or accounting of calories can affect results (2). Evaluation by a registered sports dietician can be helpful in more precisely assessing EI and EA. FFM can be obtained using DXA, bioelectrical impedance, water or air displacement plethysmography and skin fold measurements.

In athletes with oligomenorrhea or amenorrhea, other causes for menstrual disturbance should be eliminated (Table 3). Evaluation with ultrasound should be considered in an athlete with signs of PCOS: acne, hirsutism.

The initial laboratory evaluation for the triad aims to identify common causes of amenorrhea, evaluate markers of

Table 4 Laboratory studies commonly evaluated in the triad

Pregnancy test
Thyroid stimulating hormone
Follicle stimulating hormone/luteinizing hormone
Estradiol
Prolactin
Triiodothyronine (T3)
Vitamin D
Iron studies

Table 5 Indications for DXA (2,4)

Any of following
A history of DSM-V diagnosed ED
BMI <17.5 kg/m ² or <85% estimate weight
Recent weight loss of ≥10% in 1 month
Age at menarche >16
Currently or history of <6 menses/year
≥2 stress fractures/reactions
One high risk stress fracture
Prior Z-score <-2.0
Malabsorption syndrome
Chronic use of medications associated with negative effects on bone health
2 or more of the following
DE for >6 mo
BMI between 17.5–18.5 or <90% estimated weight
Recent weight loss 5–10% in 1 month
Menarche between age 15–16
Currently or history of 6–8 menses in 12-month period
One prior stress fracture/reaction
Prior Z-score between -1.0 and -2.0

ED, eating disorder; DE, disordered eating.

EA and assess levels of some nutrients important for bone health (*Table 4*). Resting metabolic rate (RMR) can also be measured to add to the assessment of EA. Low RMR or RMR/predicted RMR <0.90 may represent adaptation to low EA (2).

Bone density evaluation with DXA should be pursued in

athletes with the risk factors listed in *Table 5*. DXA testing should be performed every 1–2 years in athletes with low Z-scores or persistent risk factors to evaluate the success of treatment in improving BMD or deteriorating bone density.

Treatment

The cornerstone of treatment of the triad is restoration of adequate EA. Early intervention to restore EA is paramount in the treatment of the triad in order to prevent the most serious manifestations including osteoporosis, amenorrhea and ED (2). Improved EA has been shown to restore normal menstrual function, improve low BMD and improve endothelial dysfunction (28,32,33) (Supplementary).

A multi-disciplinary team including a physician, a registered dietician, certified athletic trainer, and, when needed, a mental-health professional is recommended. At times, coaching staff and parents may be included in the treatment process.

Improved EA can be achieved by increasing calorie intake and/or decreasing EEE. The goal of increasing EA is to increase weight and achieve the resumption of menses in order to prevent bone loss/enhance bone gains. While weight gain and return of menses can occur, in some athletes, with EA >30 kcal/kg FFM per day, EA >45 kcal/kg FFM per day may be needed to optimize improvements in BMD (3). If resources to accurately calculate EA are not available, a goal of increasing calorie intake to 20–30% more than the typical baseline needs of 2,000 kcal/day can be set (2,16). This can be attained by gradually adding 200–600 kcal/day to dietary intake (2). Ideally, increased EI is achieved with consumption of healthy, balanced food, rather than dietary supplements. Even with adequate improvements in EA, resumption of menses can take 6–12 months (34).

Regular monitoring of treatment progress is important, particularly early in treatment and the athlete should be seen by a member of the treatment team and have weight measured about once a week. Limited evidence from case and observational studies suggest that while weight gain and resumption of menses can improve BMD, complete normalization may not be possible in all athletes. In adolescents with the triad, it is especially important to intervene early, as adolescence is a critically important time for bone mass accrual.

In athletes with ED a mental health professional can address psychosocial issues related to disordered eating and cognitive behavioral therapy has been found to improve the

use of pathogenic weight control techniques and decrease the pursuit of thinness (35).

Early treatment should also include optimization of calcium and vitamin D intake with supplementation, as needed. The Recommended Dietary Allowance of calcium for children and adolescents is 1,300 mg and for adult women is 1,000–1,200 (36). RDA for vitamin D in children and adult women is 600 IU. Vitamin D intake may need to be increased in those with vitamin D deficiency or limited sun exposure (36). Other vitamins, including B vitamins, vitamin K and iron contribute to bone health.

The role of exercise in the treatment of the triad is not entirely clear. Weight bearing exercise including high impact, resistance training and some aerobic training have been shown to improve BMD in premenopausal women. Programs that include a combination of high impact training and resistance training seeming to be the most effective in improving BMD (2,9). Also, lean body mass is an independent predictor of BMD in eumenorrheic and amenorrheic adolescent athletes and non-athletic controls (9). But, there is no prospective information regarding the effects that increasing FFM might have on BMD in athletes affected by the triad. However, there is limited prospective data in anorexic women demonstrating that gains in FFM during treatment period are a positive predictor for improvements in hip and lumbar spine BMD (37). The risk for injury in athletes with low BMD with the introduction of high impact training is concerning. However resistance training could be introduced with less risk for stress fracture/injury, but the benefits are not yet established.

Improvements in BMD can take several years and BMD can be monitored with DXA every 1–2 year to evaluate for improvements.

Stabilization of or improved BMD Z-scores, improved EA, weight gain and resumption of menses are indicators of positive responses to therapy. Though return of normal menses can be delayed beyond 1 year, even with improved EA. Pharmacologic treatment strategies can be considered if there is no response to non-pharmacologic strategies after year of treatment or if new stress fractures/reactions occur during the course of treatment (2).

The psychological components of ED/DE may require pharmacologic intervention earlier (2). Antidepressants have been demonstrated to be helpful in the treatment of bulimia but not anorexia. Medications to treat anxiety, depression and obsessive compulsive disorder may also be helpful (2).

Studies evaluating the usefulness of estrogen replacement in the treatment of menstrual dysfunction and/or low BMD in the form of oral contraceptive pills (OCP) or estrogen replacement therapy (ERT) have produced mixed results, with most showing no benefit in BMD (2,4,38). The hormonal environment created with OCP and HRT does not replicate that of naturally occurring, spontaneous menstruation and first pass metabolism of oral hormones in the liver suppresses IGF-1 which may limit the antiresorptive effects of estrogen on bone (38). Furthermore, the regularly occurring cycles induced by OCP may provide the athlete with a false sense of security that EA has been restored. Unless OCP are being prescribed for other indications, they should be avoided in treatment of the triad (2,4).

Transdermal estrogen, which avoids first pass hepatic metabolism and does not suppress IGF-1, has not been studied in the triad, but has been shown to improve spine and hip BMD in adolescent athletes with anorexia nervosa (39).

Bisphosphonates are antiresorptive agents used in the treatment of postmenopausal osteoporosis. In postmenopausal women, low BMD is primarily due to increased bone resorption, while in the triad decreased bone formation plays a larger role, making bisphosphonates less likely to be effective (40). There are also concerns regarding the use of bisphosphonates in adolescents and women of child bearing age due to potential for teratogenicity. Additionally, the documented association with osteonecrosis of the jaw and atypical femur fracture in long-term use of bisphosphonates is cause for concern. The US Food and Drug Administration has not approved any pharmacologic therapies for the treatment of low BMD/osteoporosis in premenopausal women.

There is no consistent evidence supporting pharmacologic therapy in the treatment of triad disorders, as acknowledged in The Female Athlete Triad Coalition Consensus Statement, but the statement suggests that pharmacologic therapy may be considered in the circumstances listed in *Table 6* (2). Transdermal estrogen with cyclic progesterone can be considered in athletes under these circumstances (2). Other medications, such as bisphosphonates, should not be used in adolescents and should not be considered in adult women unless new fracture occurs during non-pharmacologic treatment and should not be prescribed without evaluation by an endocrinologist or other metabolic bone specialist (2).

Table 6 Consider pharmacologic therapy (2)

BMD Z-score ≤ -2.0 with a clinically significant fracture AND no response to 1 year of non-pharmacologic therapy

BMD Z-scores between -1.0 and -2.0 with a clinically significant fracture and ≥ 2 additional triad risk factors AND no response to 1 year of non-pharmacologic therapy

In athletes between 16–21 years of age, BMD Z-score ≤ -2.0 without a clinically significant fracture and at least one additional triad risk factor AND no response to 1 year of non-pharmacologic therapy

BMD, bone mineral density.

Conclusions

Low EA can present significant risk to the health of female athletes. Screening, early recognition and aggressive treatment of the triad disorders, especially in adolescent athletes, should be pursued by healthcare professionals who care for female athletes.

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Supplemental questions

1. *Dr. Robin V. West: At what age should female athletes start being screened for the triad?*

Authors' answer: Athletes can start being screened for the triad between the ages of 10–12.

2. *Dr. Robin V. West: Decreased energy expenditure and increased caloric input are often difficult for highly competitive athletes to do. How do you initially approach these athletes, and what are your first recommendations?*

Authors' answer: Now that activity trackers are inexpensive and easy to use most athletes can estimate their caloric expenditure during activity with a tracker. Most of these trackers have a calorie tracker, as well.

Without the use of a tracker, calorie expenditure estimates can be made base on the sport or activity using tables found on the web such as this site that estimates the amount of calories expended during various activities: <https://www.health.harvard.edu/diet-and-weight-loss/calories-burned-in-30-minutes-of-leisure-and-routine-activities>.

I often recommend consult with a registered dietician, as mentioned in the manuscript, particularly for athletes affected by the triad or athletes trying to gain or lose weight or alter diet to improve performance.

3. *Dr. Robin V. West: Do you manage sexually active teenagers with the triad differently than non-sexually active ones?*

Authors' answer: There is no difference, pregnancy should be considered in all athletes with amenorrhea.