REVIEW ARTICLE

Detection and Management of the Female Athlete Triad

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Low Bone Mineral Density

ABSTRACT: The female athlete triad is a disorder seen in physically active females that manifests as three interrelated syndromes that may or may not occur simultaneously.[1,2,3] It is a multi-component disease initiated by an energy deficient state (possibly from an eating disorder), bone mineral density abnormalities and menstrual changes.[1,2,3] Prevention and early intervention are important in averting permanent debilitating damage. The cornerstone of treatment is creating a positive net energy availability, which requires a multidisciplinary approach comprised of a licensed physician, nutritionist, exercise physiologist, mental health practitioner, athletic trainer, coaches, the athlete and their parents.

INTRODUCTION

In the United States alone, it is estimated that three million females participate in interscholastic sports yearly.[4] This may be due to the many physical, mental and social benefits of exercise and competition. However, there are unique physiologic and behavioral effects of excessive physical activity. As the benefits of exercise outweigh the risks, the American College of Sports Medicine (ACSM) recommends that all females participate in some sort of physical activity or sports.[2] With this recommendation of participation in sports, clinicians noticed a rise in menstrual abnormalities and non-traumatic stress fractures.[1] The ACSM noticed that these conditions were interrelated and termed them the female athlete triad.[1]

ENERGY AVAILABILITY

Energy availability is the key etiological component behind the triad.[1,2,3] The combination of exercise and inadequate caloric intake contributes to low energy availability. Energy availability (EA) is expressed as kilocalories of fat-free mass (kcal/FFM). According to the ACSM, the proportion of fat needed to maintain a healthy weight is about 5 percent for men and 12 percent for women; this means that a healthy fat-free mass for males should be between 78–90 percent lean mass and 68–80 percent lean mass for women.[5]

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Those considered at high risk for low energy states are females involved in sports that emphasize specific weight goals or aesthetics (gymnastics and ballet).[1] However, all female athletes, regardless of physical build or sport, are at risk. It is also important to consider the athlete's level of competition. As athletes progress from high school through collegiate and to an elite level of competition, the incidence of the triad increases. In one study conducted by the Norwegian Olympic Committee, it was observed that elite athletes from 66 different sports were found to have a higher incidence of menstrual abnormalities and stress fractures than the control population.[6]

Low energy availability may be the result of an eating disorder but can occur in the absence of such a diagnosis.[7] Athletes may experience low EA by inadvertently failing to meet the energy requirements of intense training due to time constraints or lack of nutritional knowledge.[7]

AMENORRHEA

The spectrum of menstrual abnormalities seen in the female athlete range from eumenorrhea, which is a typical 28-day cycle ± 7 days, to amenorrhea.[2] Amenorrhea is defined as the absence of menses for at least three months.[2] We can further differentiate amenorrhea as either primary or secondary. In primary amenorrhea, we see patients who have a delay in menstruation past 15 years of age in the setting of normal sexual development.[2,3] Secondary amenorrhea is the loss of menses after menarche.[7]

The type of amenorrhea seen in female athletes with low energy availability is functional hypothalamic amenorrhea (FHA).[7,8] With FHA, there is a suppression of the hypothalamic pituitary ovarian axis with no discernible anatomic cause. The three types of FHA are weight loss, stress and exercise-induced.[8] This occurs from irregularities in pulsatile gonadotropin-releasing hormone secretion, which results in decreased gonadal functioning.[1,2,7,8] In one randomized prospective cohort study, LH pulsatility was

disrupted abruptly at a threshold of caloric intake below 30 kcal/kg.[9] Leptin, a cytokine expressed on adipose tissue, plays a key role in up-regulating gonadotropin-releasing hormone release.[2] In patients with decreased fat mass, there is a decrease in circulating leptin, which further exacerbates menstrual dysfunction.[7] Amenorrhea, secondary to low energy availability, does not require the presence of an eating disorder. In one long term prospective study it was found that anovulation was induced in females who increased energy expenditure through exercise despite adequate nutritional status.[2]

BONE MINERAL DENSITY ABNORMALITIES

According to the National Institutes of Health, osteoporosis is classified as a state of low bone density, which predisposes patients to an increased risk of fractures.[10] We quantify one's risk for osteoporosis based on their bone mineral density.[10] It is important to understand, however, that bone mineral density is not solely responsible for patients' risk of fracture. Aside from bone mineral density, bone strength is dependent on the actual structure of the bone mineral and the quality of bone protein. The greatest development of bone mass occurs during puberty, typically between the ages of 11 and 14 years in females. In one prospective study, we see that bone formation prevails over bone resorption, resulting in a 40 percent peak bone mass during that time.[11] It is estimated that by the age of 18, young, healthy women achieve 92 percent of their total body mineral content and 99 percent by age 26.[7] Osteoporosis is not just accelerated bone mineral loss as we age but can also be secondary to poor accumulation of optimal bone mineral density during childhood and adolescence.

The International Society for Clinical Densitometry recommends that bone mineral density in children and pre-menopausal women be expressed as Z-scores.[7] The Z-score shows the bone mineral density of an individual as the number of standard deviations from the mean for an age matched, population specific patient. An acceptable Z-score for normal bone mineral density of any age range is greater than -2.0. Those below -2.0 are classified as below the expected range for age.[7] Osteoporosis is diagnosed in childhood when a child is in the bottom 5th percentile for bone density for their respective age and has a history of recurrent fractures.[7]

Healthy female athletes tend to have higher bone mineral densities when compared to non-athletic females.[2] Weight-bearing exercises are beneficial in bone development and architecture. However, despite similar weight-bearing exercises, female athletes with low energy availability and amenorrhea tend to have lower bone mineral densities.[2] In one study, amenorrhea observed in female athletes was associated with decreased bone mineral density in the lumbar spine.[7] The hypogonadal state appears to play a major role in promoting lower bone mineral density. Estrogen plays a significant role in the regulation of bone mass by its effects on human growth hormone, as well as osteoblast and osteoclast function.[1,2] Low estrogen states, as seen in amenorrhea, cause a decrease in osteoclasts' inhibition leading to increased bone breakdown.

SCREENING AND DIAGNOSIS

The diagnosis of the female athlete triad can be difficult. Some of the health consequences related to the disorder are not typically apparent. The optimal time to assess elements associated with the triad is at the pre-participation physical examination.[1,2,7] Any athlete who presents with a component of the triad should be screened for the other components. The 2014 Consensus Panel recommended that female athletes undergo annual screening with a triad-specific self-reported questionnaire displayed in Table 1.[3]

TABLE 1:

Triad consensus panel screening questions

1. Have you ever had a menstrual period?
2. How old were you when you had your first menstrual period?
3. When was your most recent menstrual cycle?
4. How many periods have you had in the last 12 months?
5. Are you presently taking any female hormones?
6. Do you worry about your weight?
7. Are you trying to or has anyone recommended that you gain or lose weight?
8. Are you on a special diet or do you avoid certain types of foods or food groups?
9. Have you ever had an eating disorder?
10. Have you ever had a stress fracture?
11. Have you ever been told you have a low bone density (osteopenia or osteoporosis)?
De Souza, Mary Jane, Native, Aurelia, Joy, Elizabeth, Misra, Madhusmita, Williams, Nancy I., Mallinson, Rebecca J, Gibbs, Jenna C, et al. (2014). 2014 Female Athlete Triad Coalition Consensus Statement on Treatment and Return to Play of The Female Athlete Triad. British Journal of Sports Medicine, 48(289)

Obtaining a detailed history regarding each component of the triad should be addressed at each visit. An accurate menstrual history includes age at menarche, provides clinicians a baseline of patients' menstrual status. When evaluating, it's important to know if menstrual cycles were eumenorrheic at baseline and if there has been any deviation from normal. There is no single lab test available to determine functional hypothalamic amenorrhea. Typically, FHA is a diagnosis of exclusion once other causes of amenorrhea have been ruled out. Initial lab work should include urine pregnancy testing, LH, FSH, prolactin and TSH.[1] LH and FSH allows us to evaluate for ovarian failure. The ratio between the two hormones provides insight into whether the patient may have polycystic ovarian syndrome (PCOS).[7] Clinical findings of excess androgen secretion (i.e., hirsutism) can also give clues toward a diagnosis of PCOS.[1,7] In FHA, LH and FSH are usually normal-low and estradiol is low.[7] Typically, TSH and prolactin are in normal range.[7]

Eating disorders tend to be more difficult to diagnose. It is one of the most under-diagnosed disorders in the United States.[2] Most patients do not present to their primary care providers with the chief complaint of an eating disorder. Inquiring about eating disorders is challenging. It requires skillful interview techniques as well as a strong interpersonal relationship with the patient. Clinicians can perform a personalized, structured interview based upon the patients eating habits or can have patients complete questionnaires such as the eating disorder examination questionnaire (EDE-Q).[1] The EDE-Q has shown to be reliable in the assessment of eating disorders; however, they tend to be time-consuming. In a busy primary care office, it may be impractical to complete an EDE-Q with each patient with a suspected eating disorder. Therefore, a brief questionnaire called SCOFF could be utilized. The SCOFF questionnaire (Table 2) is a quick and easy to remember acronym that is reliable in detecting eating disorders.[1] Any score greater than or equal to two indicates a likely diagnosis of anorexia nervosa or bulimia.[12] Initial laboratory workup should include a chemistry panel, CBC with differential, ESR, thyroid function and urinalysis.[2] Also, an EKG should be obtained as patients identified as having an eating disorder have prolonged QT intervals, even in the setting of normal electrolytes.[13] The QT prolongation improved after re-feeding.[13]

Bone mineral density should be assessed in any female athlete who is presenting with a history of recurrent stress fractures or fractures with minimal trauma. Also, if there is a six-month history of amenorrhea, oligomenorrhea or eating disorder, a bone mineral density assay should be obtained.[1] Bone mineral density assessment is done by dual-energy x-ray absorptiometry (DXA).[1,2,7] Diagnosis is made with a low Z-score of either a PA view of the spine or the hip. Both sites are evaluated and whichever has the lowest Z-score is what is used as the actually measured score.[1] It is recommended that patients under the age of 20 obtain a whole body DXA and PA x-ray of the spine.[1,2] A Z-score of less than -2.0 confirms the diagnosis of low bone mineral density for expected age.[2] It is recommended that after medical management a repeat DXA should be conducted in 12 months.[2]

MANAGEMENT

The first goal of treatment should be to increase total energy availability by either decreasing energy expenditure or increasing dietary energy intake.[1,2,7] A multidisciplinary approach is necessary for recovery. Increasing energy availability has been shown to restore normal menses and improve bone mineral density.[1,2] It is estimated that the female athlete may need to increase energy availability to a minimum of 30 kcal/kg of lean mass per day to normalize menses. Per the ACSM, the recommended energy intake for a sedentary female is roughly between 1800–2000 kcal/d; an additional 500–1000 kcal/d is added for active females.[1] The dietician and patient should devise a meal plan that focuses on the patient's estimated energy requirement. This is based on an individual's energy intake, expenditure, age, sex, weight, height and physical activity level.

Many athletes are not as open to alterations in exercise intensity and duration. Therefore, nutrition should be the primary focus to help increase energy availability. Although research is limited, supplementation of vitamin D, vitamin K and calcium can be added.[1] Increasing energy availability should continue to be the focus of management until normal menses resume.

TABLE 2:

The Scoff questionnaire: a screening tool for eating disorders

1. Do you make yourself sick because you feel uncomfortably full?
2. Do you worry you have lost control over how much you eat?
3. Have you recently lost more than one stone (14 lbs) in a three-month period?
4. Do you believe yourself to be fat when others say you are too thin?
5. Would you say that food dominates your life?
**One point for every "yes"; a score of ≥ 2 indicates a likely case of anorexia nervosa or bulimia?*

Overcoming the psychological component of their disorder seems to be the biggest hurdle towards recovery. Athletes are driven individuals who are goal-oriented and look for success regardless of damages that could be done to their health. Altering an athlete's perception and mentality offers a difficult challenge. It is important to utilize the assistance of a mental health clinician to help overcome specific mental barriers towards recovery. Personal contracts appear to have shown positive results in the goals of treatment. If certain parameters of the personal contract are not met (i.e., dietary intake of 2000 kcal/d), the patient may have to abstain from competition or training.[1]

PHARMACOLOGICAL CONSIDERATIONS

There is very little evidence for pharmacological management as a standard of treatment for the triad. Typically, once the weight is restored, most patients are started on SSRIs for management of their eating disorder if present.[2] There is no one pharmacologic agent that can be used to treat functional hypothalamic amenorrhea. Oral contraception (OCPs) has been shown to normalize menses, but it is important to recognize that metabolic factors that impair bone health are still relevant.[2] Some studies now suggest that transdermal estrogen therapy may have a better impact on bone health. However, most research is limited to postmenopausal women.[7,14]

In one randomized double-blinded study of 110 females with diagnosed anorexia nervosa, it was found that for those patients prescribed transdermal 17-β estradiol, bone mineral density increased in both the spine and hip.[14] The benefit of using transdermal estrogen is that it has little to no effect on insulin-like growth factor, as opposed to OCPs that have relatively high levels of estrogen, which further suppress IGF-1.[14] Insulin-like growth factor is an important bone trophic hormone secreted by the liver and is typically suppressed in patients with FHA.[8,14] Bisphosphonates that are approved for management of low bone density in postmenopausal women should not be used in young female athletes with functional hypothalamic amenorrhea.[1] Bisphosphonates tend to remain in bones for years and their teratogenic potential should be avoided in women of child-bearing age.[1,2]

TABLE 3:

Return to play risk stratification protocol worksheet

RISK FACTORS	LOW RISK - 0 POINTS EACH	MODERATE RISK - 1 POINT EACH	HIGH RISK – 2 POINTS EACH
Low EA with or without eating disorder	[ ] no dietary restrictions	[ ] some dietary restriction	[ ] meets DSM-V criteria for ED
Low BMI	[ ] BMI ≥ 18.5 or ≥ 90% EW or weight stable	[ ] BMI 17.5 < 18.5 or <90% EW or 5 to <10% weight loss/month	[ ] BMI ≤17.5 or <85% EW of ≥ 10% weight loss/month
Delayed menarche	[ ] menarche < 15 years	[ ] menarche 15 to <16 years	[ ] menarche ≥ 16 years
Oligomenorrhea and/or amenorrhea	[ ] > 9 menses in 12 months	[ ] 6-9 menses in 12 months	[ ] <6 menses in 12 months
Low bone mineral density	[ ] z-score ≥ -1.0	[ ] z-score -1.0 <2.0	[ ] z-score ≤ -2.0
Stress fracture	[ ] None	[ ] 1	[ ] ≥ 2; ≥ 1 high risk or of trabecular bone site
Cumulative risk	**____ points +**	**____ points +**	**___ points = ____ Total**

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Currently, the best approach for management is early detection and prevention. Strong efforts should be made to educate patients, medical staff, coaches and educational institutions on how to optimize energy availability best and prevent injury. Pre-participation physicals provide the best time to screen for symptoms associated with the triad.[1,2,7]

RETURN TO PLAY CONSIDERATION

To date, there is no standardized clearance or return to play guidelines. According to the ACSM 2012 consensus statement, the physician's goal is to return an uninjured athlete to practice or competition without putting that individual at undue risk.[9] The consensus panel recommends a risk stratification protocol be followed to guide clinicians when to allow athletes back to competition.[3]

Table 3 outlines the risk stratification protocol worksheet. Patients who score 0–1 points are considered low risk for injury and can be granted full clearance. A score of 2–5 points puts the patient at moderate risk and would require limited clearance. Any patient with a score of 6 or higher is restricted from further training or competition. It is important to recognize that recovery for each component of the triad is different. Increasing energy availability positively affects metabolic function within days to weeks. Menses can typically resume within several months but could take up to one year. Bone mineral density recovery occurs over a more extended period and can usually take several years to restore.[3]

CONCLUSION AND FUTURE CONSIDERATIONS

The female athlete triad is a multi-component disorder comprised of low bone mineral density, menstrual abnormalities and eating disorders. Any female who presents with one component should prompt a more comprehensive workup. Once identified, the most important initial step towards recovery is increasing energy availability, either through dietary intake or decreasing energy expenditure. Management requires a multi-component therapy team comprised of physicians, mental health therapists, athletic trainers, nutritionists, coaches and educational administration. Increased education in recognition of signs and symptoms associated with the triad is needed to facilitate prompt diagnosis and prevention.

The International Olympic Committee recently provided updates to the female athlete triad to include a broader list of health consequences deemed relative energy deficiency in sports (RED-S).[15] The purpose was to show how males also can present with analogous symptoms. Most of the clinical symptoms are parallel to what we would see in the female athlete triad. However, RED-S looks to address aspects of physiologic function including metabolic rate, menstrual function, bone health, immunity, protein synthesis, cardiovascular and psychological health.[15]

AUTHOR DISCLOSURES :

The author(s) declare no relevant financial affiliations or conflicts of interest.

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