Revisión
Energy availability, menstrual dysfunction and bone health in sports; an overview of the female athlete triad
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Abstract

Introduction: The female athlete triad (FAT) is a serious health-related problem that threatens women who exercise. This condition is an interrelated multifactorial syndrome which includes low energy availability, menstrual cycle disturbances and decreased bone mineral density.

Objective: To review the major components of the FAT and their relationships, as well as strategies for diagnosis and treatment.

Methods: Articles related to the topic were reviewed through PubMed and SportDiscus databases.

Results: Interrelationship between components of the FAT may result in clinical manifestations, including eating disorders, amenorrhea and osteoporosis. Clinical conditions are not always exhibited simultaneously. Prevention is important to minimize complications. Diagnosis and treatment is complicated and often must involve an interdisciplinary therapeutic approach.

Conclusions: Understanding of the disease may be facilitated by a unified framework focusing on energy deficiency. Preventive or early interventions require to increase energy availability through a higher total energy intake or a decrease in energy expenditure trough excessive physical exercise. A healthy lifestyle, and support by parents and coaches should be included. Psychotherapy may be necessary when eating disorders are present.

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Key words: Female athlete. Energy availability. Eating disorders. Menstrual disturbances. Osteoporosis.

Resumen

Introducción: La tríada de la atleta femenina es un importante problema de salud que amenaza a las mujeres que practican ejercicio. Este trastorno constituye un síndrome multifactorial e interrelacionado que incluye una baja disponibilidad de energía, alteraciones del ciclo menstrual y disminución de la densidad mineral ósea.

Objetivo: Revisar los componentes de la tríada de la atleta femenina y sus interacciones, así como las estrategias de diagnóstico y tratamiento.

Métodos: Se revisaron artículos relacionados con el tema en las bases de datos Pubmed y Sportdiscus.

Resultados: La interrelación entre los componentes de la tríada de la atleta femenina puede resultar en condiciones clínicas, como trastornos alimentarios, amenorrea y osteoporosis. Estas condiciones no siempre se presentan de forma simultánea. La prevención es importante para minimizar las complicaciones. El diagnóstico y el tratamiento son complicados y a menudo requieren un enfoque terapéutico multidisciplinar.

Conclusiones: El conocimiento de la enfermedad puede facilitarse por medio de un marco unificado centrado en la deficiencia de energía. Las intervenciones preventivas y tempranas requieren un incremento de la disponibilidad de energía a través de un mayor aporte energético o una reducción del gasto asociada a un ejercicio físico excesivo. Se debe incluir un estilo de vida saludable y el apoyo por parte de padres y entrenadores. La psicoterapia puede ser necesaria si se presentan trastornos alimentarios.

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Abbreviations

ACT: Acceptance and commitment therapy.
DSM: Diagnostic and Statistical Manual of Mental Disorders
BMD: Bone mineral density.
CBT: Cognitive behavioral therapy.
CRH: Corticotrophin releasing hormone.
DXA: Dual-energy X-ray absorptiometry.
EDNOS: Eating disorder not otherwise specified.
FAT: Female athlete triad.
FED: Female energy deficiency.
FMD: Flow-mediated dilatation.
FSH: Follicle stimulating hormone.
GnRH: Hypothalamic gonadotrophin-releasing hormone.
GH: Growth hormone.
IGF: Insulin-like growth factor.
ISCD: International Society for Clinical Densitometry.
LH: Luteinizing hormone.

Introduction

Over the last few decades social changes have fostered the development of a positive attitude towards female athletic activities, and there has been a dramatic increase in the number of girls and women participating in all levels of sports competitions. For most individuals this is a positive experience which provides improved physical fitness and better health. However, female athletes have also developed their own unique set of medical problems, being the Female Athlete Triad (FAT) one of the most relevant. Association of diminished bone mineral density (BMD) to amenorrhea was described in female athletes in 1987, and FAT, characterized by the presence of an eating disorder, together with amenorrhea and osteoporosis, was first documented twenty years ago. The FAT was officially recognized in a position stand issued by a panel of experts conveyed by the American College of Sports Medicine (ACSM) in response to the increase in stress fracture rates, decreases in BMD, and menstrual dysfunction in otherwise healthy female athletes. This syndrome is now recognized as a complex set of inter-relationships between energy availability, menstrual status, and bone mineral density, which may have a variety of clinical manifestations, including eating disorders, functional hypothalamic amenorrhea, and osteoporosis. The ACSM published a new position stand in 2007, in which recommendation for screening, diagnosis, prevention, and treatment were proposed. More recently, a position stand on this subject also been provided by the International Federation of Sports Medicine.

This review aims at providing an overview of our current understanding in relation to the major components of the FAT and their relationships, as well as to analyze strategies for the management of patients with this complicated condition.

Components of the FAT

The FAT stars with low energy availability (with or without eating disorders), which in turn causes amenorrhea and a reduction in estrogen levels that eventually leads to bone loss. An athlete's condition moves between health and disease along the spectrum of these interrelated conditions according to her diet and exercise habits, and FAT should be evaluated as a continuum rather than as a disorder consisting of three concise components. Each individual component and the full range of the FAT, according to the ACSM is shown in figure 1.

Energy availability and eating disorders

Energy availability is the amount of dietary energy for all physiological functions after accounting for energy expenditure from exercise, that is, the amount of remaining energy available for other body functions after exercise training. In young healthy individuals, energy balance occurs at a energy availability around 45 kcal per kg of free fatty mass per day. When values are under 30 kcal per kg of free fatty mass per day, the reproductive function and bone formation are reduced to restore energy balance, resulting in an impairment of reproductive and skeletal health.

Low energy availability may result when exercise energy expenditure increases more than energy intake, as may occur in endurance sports, but also appears when energy intake is reduced more than exercise energy expenditure. Female athletes in sports such as gymnastics, ballet dancing, or figure skating, in which leanness and aesthetics are emphasized, fit into a risk profile for FAT, and may develop poor nutritional behaviors such as food restriction, binging or purging, laxative, enema or diuretic abuse, and excessive exercise, resulting in low energy availability. Although the presence of disorders of eating behavior is not necessary to initiate the cascade of deleterious effects that result from the FAT, energy availability expresses in some athletes as eating disorders, characterized by abnormal eating behaviors, an irrational fear of gaining weight, and false beliefs about eating, weight, and shape. Eating disorders are potentially chronic conditions associated with a range of medical, psychological, and psychosocial consequences. Anorexia Nervosa represents the extreme of restrictive eating behavior in which the individual views herself as overweight and feels terrified of gaining weight, even though being 15% or more below ideal body weight. Individuals with Bulimia Nervosa, on the other hand, are characterized by repeated cycles of uncontrolled
bingeing followed by purging through vomiting, diuretics, enemas, the use of laxatives, and excessive exercise.\textsuperscript{13} Anorexia nervosa and bulimia nervosa have been classically diagnosed according to the definition by the (APA) Psychiatric Association in the fourth edition of \textit{Diagnostic and Statistical Manual of Mental Disorders} (DSM-IV).\textsuperscript{14} As stated in the DSM-IV, the diagnosis of anorexia nervosa requires four criteria: refusal to maintain weight within a normal range for height and age, intense fear of gaining weight or getting fat, severe body image disturbance or denial of the seriousness of the current low body weight, and absence of the menstrual cycle for greater than three cycles in postmenarchal women. The criteria for bulimia nervosa include recurrent episodes of binge eating with a sense of lack of control, recurrent inappropriate compensatory behavior to prevent weight gain, the binge eating and compensatory behavior to occur at least twice per week for three months, and self-evaluation unduly influenced by body shape and weight. Anorexia is further divided into restricting and binge eating/purging subtypes, and bulimia into purging and nonpurging subtypes.\textsuperscript{14} Individuals who do not meet the criteria for anorexia nervosa or bulimia nervosa are classified as having an Eating Disorder not Otherwise Specified (ED-NOS); they often have a normal body weight, but are focused on body image, weight, and guilt surrounding eating.\textsuperscript{14}

In the sport medicine field some researchers have also introduced the term \textit{Anorexia Athletica}, to refer to a disordered eating pattern seen in the female athlete who has an intense fear of gaining weight even though she is underweight. This condition is more frequently seen in sports where an individual body weight is a precondition for a high performance rating. Women with anorexia athletica reduce their energy intake and exercise excessively, and may display features of anorexia nervosa without meeting strict diagnosis criteria.\textsuperscript{17} This disorder has been defined as a continuum model spanning between the two clinical disorders anorexia nervosa and EDNOS.\textsuperscript{18} Wheatley et al.\textsuperscript{19} have recently summarized the key characters of anorexia athletic and FAT in comparison to anorexia nervosa and EDNOS, and proposed a new unified framework, under the term \textit{Female Energy Deficiency} (FED), to reconcile overlapping definitions.

Eating is regulated by the neuroendocrine systems in which the hypothalamus-pituitary-adrenal axis plays a major role. The adipocyte-derived hormone leptin, which has an inhibitory effect on appetite, has been implicated in eating disorders\textsuperscript{20} and, although the responsible mechanism still needs to be elucidated, recent research suggests that leptin level is an important indicator of energy deficiency, reflecting the dietary status and caloric balance.\textsuperscript{21}

In addition to the presence of the other two components of the FAT -amenorrhea and decreased bone density- medical complications associated with disordered eating include decreased lean body mass, depleted glycogen stores, chronic fatigue, micronutrient deficiencies, anemia, dehydration, erosion of tooth enamel, gastrointestinal disorders or electrolyte and acid-base imbalances. Psychological problems,
Menstrual status

Menstrual dysfunction in the female athlete includes a wide spectrum of disorders. The most commonly discussed is amenorrhea, or absence of menstrual cycle, that can be divided into primary and secondary. Primary amenorrhea, or delayed menarche, may be present in female athletes who begin training before puberty, and is defined in an athlete with absence of menstruation by the age of 15. Secondary amenorrhea occurs in postmenarchal athletes who lack three or more consecutive cycles after menarche, and is not pregnant.\textsuperscript{22} In female athletes is also frequent the occurrence of irregular cycles or oligomenorrhea (six or fewer cycles per year).\textsuperscript{7} Anovulation and luteal phase deficiency, with ovulation but inadequate progesterone support for endometrial development, may also occur.\textsuperscript{23}

Menstrual cycle problems result from the suppression of the pulsatile secretion of hypothalamic gonadotrophin-releasing hormone (GnRH), which leads to a reduced secretion of luteinizing hormone (LH) and follicle stimulating hormone (FSH), thus preventing ovarian stimulation, and causing a fall in the levels of estrogens and progesterone. One of the earliest theories on menstrual dysfunction in female athletes theorized that onset of menarche requires a critical threshold on body fat (17% of body weight) to be reached. Under this critical percentage of body fat the metabolic rate decreases and the sensitivity of the hypothalamus to gonadal steroids would be altered.\textsuperscript{24} However, more recent research has challenged the theory of dependence on critical body weight or fat percentage.\textsuperscript{25} Psychological stress has also been implicated in the aetiology of exercise-related menstrual disturbances, but few data seem to support this hypothesis, and amenorrheic athletes exhibit a similar psychological profile to menstruating athletes.\textsuperscript{24}

Although specific signals and pathways have yet to be identified, the aetiology of functional hypothalamic amenorrhea associated with exercise and stress could be mainly a consequence of the inhibition of GnRH release and the lost of LH pulsatility, dependent on low leptin levels. In addition to regulating appetite and energy availability, leptin is known to centrally act to influence reproduction, exerting its effect over a narrow range of concentrations. Leptin concentration responds to a negative energy balance, and it seems that menstruation is not possible if leptin levels drop under a critical level.\textsuperscript{26} Thus, menstrual dysfunction is not caused by stress or a low proportion of body fat, but results from the disruption of the GnRH pulse generator as a consequence of low energy availability.\textsuperscript{27} A relatively large number of studies have confirmed that energy balances is generally more negative and overall energy availability lower in adult athletes with menstrual dysfunction compared to eumenorrheic controls.\textsuperscript{28} Another hormone that affects GnRH pulsatility is ghrelin, an anorexigenic peptide which may help to explain why women who have regained normal weight or who have ceased to exercise, but still show distorted eating patterns, can have prolongation of amenorrhea.\textsuperscript{27} Recent research also suggests a potential role for adiponectin, a hormone whose levels rise with prolonged fasting and weight reduction. It is known that adiponectin reduces basal and GnRH-stimulated LH secretion,\textsuperscript{28} and the high levels of adiponectin present in lean and energy restrained female athletes could contribute to chronic anovulation.\textsuperscript{24}

Additional hormones which apparently contribute menstrual cycle dysfunction and may influence GnRH release are glucocorticoids and catecholamines, which inhibit gonadal function in response to the stress of exercise.\textsuperscript{\textsuperscript{19}} Various other hormones, such as corticotrophin releasing hormone (CRH), growth hormone (GH), insulin-like growth factor (IGF)-1, thyroxine or melatonin could also play a role.\textsuperscript{23,26}

Hormonal alterations may cause multiple complications, including not only effects on BMD, but also damage and inadequate repair of soft tissue, inhibition of immune and thyroid function, lost of the cardioprotective effects on lipids and vessel walls, or changes in renal function.\textsuperscript{26,29}

In addition, lack of stimulation of estrogen receptors in the vessels results in impaired endothelium-dependent arterial vasodilatation.\textsuperscript{6} A few studies have documented a detrimental relationship between athletic amenorrhea and brachial arterial dysfunction, and decreased flow-mediated dilatation (FMD) has been reported in amenorrheic female collegiate runners, endurance athletes.\textsuperscript{30} This has been confirmed in a study performed on professional ballet dancers in which correlations between abnormal FMD and estrogen levels or low BMD were observed.\textsuperscript{31} Evidence makes endothelial dysfunction a potential forth component of the FAT.\textsuperscript{32}

Bone health

The last component of the FAT is best described as a spectrum encompassing optimum bone health, low BMD, and osteoporosis (fig. 1). Osteoporosis in female athletes refers to premature bone loss and inadequate bone formation, resulting in low BMD, microarchitectural deterioration, increased skeletal fragility, and increased risk of stress fractures.\textsuperscript{7,24} Physical exercise has a positive effect on bone accrual and architecture, and healthy athletes may have a higher BMD than nonathletic individuals.\textsuperscript{33} However, it is known that amenorrheic athletes have lower BMD than their eumenorrheic counterparts.\textsuperscript{34} Therefore, factors contributing to menstrual dysfunction can put athletes at risk for compromised bone health and for the development of abnormally low BMD (osteopenia) and osteoporosis.\textsuperscript{33}
Estrogen helps to the maintenance of BMD by influencing calcium absorption, bone formation and remodeling. Estrogen has a direct effect on osteoblasts by increasing cell proliferation and proteins that alter bone remodeling, and also inhibits the production of cytokines associated with bone reabsorption. In addition to a decrease in hormone concentration, other components of the FAT may directly or indirectly affect bone mass. Thus, low energy availability or restricted energy intake may result in an inadequate intake of macronutrients, such as essential amino acids and fatty acids, or mineral and vitamins, such as calcium and vitamin D, which are required for bone health. Low energy availability may also impair bone formation through effects on other hormones such as cortisol and leptin.

Athletes suffering from menstrual cycle disturbances are especially at risk for stress fractures, whose incidence has been reported to be higher among amenorrheic and oligomenorrheic as compared to eumenorrheic athletes. The risk of stress fractures is increased by factors such as age, BMD, prior exercise training and alcohol, but not by age of menarche or oral contraceptive use. The most common site of stress fractures in women is the tibia, accounting for 25% to 63% of cases.

Moreover, even if athletes under treatment return to a normal reproductive status, no long-term study has demonstrated that lost BMD can be fully regained. Because peak bone mass is reached by the third decade of life, the problem is especially critical for adolescent athletes.

**Prevalence of the disease**

Because the FAT is considered a continuum, identifying prevalence values can be difficult. Nevertheless, research suggests that 1% to 3% of female athletes meet the three criteria for FAT. According to the ACSM there are some sport disciplines at a higher risk for developing one or more components of the FAT. These are: sports in which performance is subjectively scored (dance, gymnastics, figure skating); endurance sports favouring participants who have a low body weight (distance running, cycling); sports in which body contour-revealing clothing is worn for competition (swimming, diving); sports using weight categories for participation (wrestling, martial arts); and sports in which prepuberal body habitus favors success (gymnastics figure skating).

Compared to the prevalence of 0.5% to 1% for anorexia nervosa, and 1% to 4% for bulimia nervosa in the general population, the prevalence of disordered eating in female athletes ranges from 1% to 62%, depending on the sport, and being higher in sports in which low body weight conveys a competitive advantage. There is a large study which examined 263 Australian elite athletes and the same number of nonathletes according to the DSM-IV criteria, eating disorders were present in 31% of athletes in “thin-build” sports compared with 5.5% of the controls. In a group of 1620 Norwegian athletes, 25% of female athletes competing in aesthetic sports, endurance sports, and weight-class sports had clinical eating disorders. More recently, a cross-sectional study of Brazilian swimmers identified a 44% of athletes meeting the criteria for disordered eating. Interestingly, results from long-term follow-up studies performed in Norway since 1993 indicate an increase in the prevalence of clinical eating disorders observed during the investigated period for female elite athletes as a group.

The range of reproductive abnormalities, including delayed menarche, oligomenorrhea, and primary and secondary amenorrhea is 6 to 79% of women involved in athletic activity, and the prevalence varies with the sports and levels of competition. Secondary amenorrhea has been reported up to 69% of ballet dancers and 65% of long distance runners. In distance runners, it has been found that the prevalence of amenorrhea increases from 3% to 60% as training distance increases from less to 13 to more than 113 km. Asymptomatic menstrual disorders, such as anovulation and luteal phase deficiency, are also common, and have been reported to occur at least one every three months in 78% of runners with regular menstrual cycles. Ballet dancing is also accompanied by a higher incidence of delayed puberty and primary amenorrhea. In gymnastics, both rhythmic and artistic, intensive physical training an negative energy balance have been shown to prolong the prepuberal stage and delay puberal onset.

The prevalence of reduced bone mineral density in athletes widely varies, osteopenia ranging from 22% to 55%, and osteoporosis spanning 0% to 13%. Differences partly reflect criteria used from different organizations and most percentages given in the literature are based on T-scores, which compare dual-energy X-ray absorptiometry (DXA) results of postmenopausal women to young adult women, while more recently research utilizes Z-scores, which compare DXA results among age-matched peers. The ACSM incorporates in its position stand the recommendations of the International Society for Clinical Densitometry (ISCD), and proposes to define low BMD in an athlete as a Z-score between -1 and -2 along with clinical risk factors for fracture, and osteoporosis as a Z-score lower than 2 with clinical risk factor for fracture. The prevalence of stress fractures in athletes diagnosed with low BMD and menstrual dysfunction may approach a rate of 17%.

Although one of the components of the FAT may be identified in a significant number of female athletes, only a few actually suffer from all three components of the triad. Thus, a study of 112 United States college athletes participating in seven different sports found that in total ten athletes met the criteria for combination of two disorders and one athlete for all three disor-
To maximize therapeutic effectiveness, treatment requires a multidisciplinary approach with support from primary care and/or sport physicians, as well as nutritionists or dietitians, psychiatrists or psychologists, coaches, and family members. Team members must identify conditions that may have contributed to the symptoms and try to address these issues. The first step should be to help eliminate the “win-at-all-costs mentality”, and the modification of the diet and exercise regimes. Because energy availability is the key aspect in the onset of the FAT, it is very important, as emphasized by the ACSM position stand, \(^4\) to determine if intake energy is insufficient in order to increase total calories intake, and to assess is a decrease in training intensity and volume is required. A desirable approach is to improve energy intake, to reduce exercise energy expenditure or, both, without dramatic changes in weight. \(^5\) This would be normally sufficient to get a positive energy balance, helping to restore regular menstruation and to prevent further bone loss. Although a general pattern does not exist, athletes may need to increase energy availability to at least 30 kcal per kilogram of fat-free mass per day to reestablish regular menstruation. \(^7\)

Nutritional education and counseling is enough for more athletes. However, the presence of clinical eating disorders requires management by mental healthcare professionals, with psychiatric medical prescription or psychotherapy, when necessary. \(^3\) Cognitive behavioral therapy (CBT) is effective in patients with bulimia nervosa, but appears to be unsupportive in other cases. This has led to the development of enhanced behavioral cognitive therapy (CBT-E), a transdiagnostic approach applicable to all types of eating disorders. \(^3\) Other recent approaches with promising results are acceptance and commitment therapy (ACT), and dialectical behavior therapy (DBT). \(^2\) Patients under treatment for eating disorders should agree to comply with treatment strategies, to be closely monitored and to modify characteristics of training, if so required, to avoid being restricted or excluded from training and competition. \(^4\) As training continues, adjustments may be necessary to maintain a balanced regime specifically designed for the athlete. \(^6\)

If athletes are resistant to initiate or maintain treatment through changes in their diet or training regime, drug interventions or hormonal supplementation could be considered to help restores menstruation and improve BMD. \(^6\) Oral contraceptive pills containing estrogen and progestin, transdermal estrogen, or leptin analog administration have been tested, although further research is required to confirm their utility as treatment options in the FAT. \(^7\) Additional measures for bone health include optimization of vitamin D (> 1,200 ng per day) and calcium intake (> 400 IU per day). \(^5,9\) Other pharmacological agents approved for treatment of postmenopausal osteoporosis, such as bisphosphonates, are not recommended. \(^4\) The use of mechanical stimulation through pulse electromagnetic field or vibratory platforms could be useful to treat bone loss, although correct dose and effectiveness require to be established. \(^4\) Finally, acid supplementation may be an effective treatment for endothelial dysfunction, but large-scales studies are still needed to inform its positive effects. \(^3,12\)

Preventive aspects are essential and must involve the entire health-care team. \(^6\) Athletes, parents and coaches should be educated about what the FAT is, how to recognize signs, and how to take steps for prevention, before this condition causes irreversible health problems. \(^3\) All must understand that the body has no mechanisms for automatically adjusting energy intake to energy expenditure by the working muscle. \(^7\) Preventive measures should include optimization of energy availability, maximization of bone mineral accrual \(^9\) young athletes, and counseling on nutritional requirements according to age. Moreover, sport administrators should also consider rules to discourage unhealthy weight loss practices. \(^4\)

Conclusions and perspectives

The FAT is an increasingly prevalent condition which involves low energy availability, menstrual dysfunction and bone health in sports.
cycle disturbances and decreased BMD. The main element underlying all the aspects of the FAT is low energy availability, so that loss of caloric balance results in menstrual dysfunction and, therefore, inadequate estrogen production and loss of bone health. Further research is necessary to establish the importance of the decreased capacity for arterial vasodilatation in amenorrheic athletes, and to establish if an expanded view of the components of the FAT may be appropriated.

Because disorders of the FAT associate with serious, potentially life-threatening consequences, prevention and early treatment are necessary to maintain the athlete’s health and to avoid sequelae. A team approach is essential, with each professional given a role in dealing with a particular aspect of the FAT and keeping lines of communication with the other.

Given the importance of low energy availability for the onset of the FAT, and the necessity for early prevention of energy deficiency, the prevailing concept of the FAT has been recently challenged, and a unified framework that, under the term FED, would include the expanded FAT and related concepts such as anorexia athletic and facilitate successful intervention, has been proposed. Future research and advances in our understanding of this multifaceted syndrome may benefit from the new suggested framework.

References


