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Key Points

- Due to anatomical, physiological and hormonal differences, women are more prone to develop some exercise-related diseases, such as *musculo-skeletal*, *hormonal* and *haematological* disorders.
- The female athlete triad is a connection between *low energy availability*, *functional hypothalamic amenorrhoea* and *osteopenia/osteoporosis*. This model may explain several disorders of women practising sports at a competitive level.
- Women are more likely to suffer from knee ligament injuries, namely, *anterior cruciate ligament (ACL) injuries* and *patellofemoral pain (PFP)*, than men.
- *Iron deficiency* frequently occurs in sporting women, with a prevalence up to 50% in sporting adolescents. The main consequence of this deficiency is anaemia that adversely affects performance and quality of life.
- Preventative measures consisting in *exercise-based interventions*, *training adaptation* and *dietary optimisation* can efficiently prevent (and treat) exercise-related hormonal and haematological disorders and musculoskeletal injuries in women practising sports.

12.1 Introduction: Women, Sport and Medicine

There is a rapidly mounting interest in defining the differences between male and female adaptations to physical activity and sport demands, largely because the history of women and sport is much younger than that of men. For example, the first

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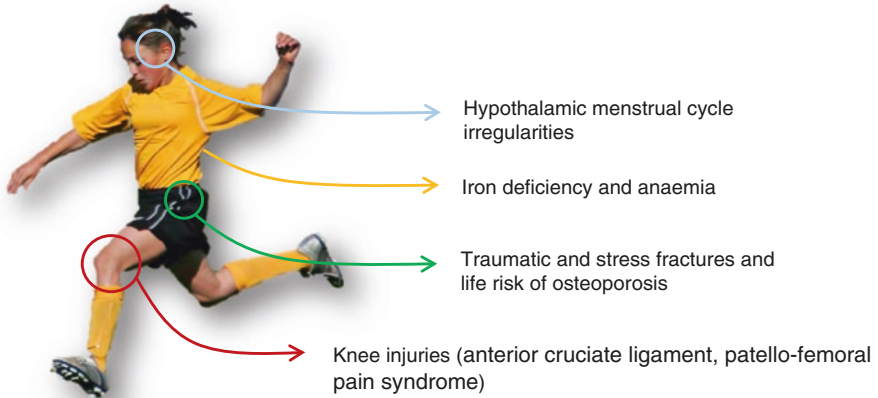


Fig. 12.1 Sport-related clinical conditions that are specific or more common in women than in men

women's Olympic marathon was held in 1984, nearly 90 years after the first modern male Olympic marathon. Therefore, studies on women's health/diseases in relation to physical activity and sport represent a relatively new branch of medicine.

The increasing number of female athletes all over the world, some of them involved in high-impact sports such as football (nearly 30 million women worldwide practise football) [1], is a strong drive to study and apply evidence-based practices to female practising sports.

Due to anatomical, physiological and hormonal differences between genders, women are more prone to develop some acute and chronic pathologic conditions related to sport demands. For instance, women have an increased likelihood of developing sport-related anaemia and of suffering from osteo-articular injuries, particularly of the legs (Fig. 12.1).

This chapter gives an overview of the most frequent sport-related disorders threatening women's health and provides information about the prevention of these conditions and the management of female athletes through their whole life.

12.2 Musculoskeletal and Ligament Injuries

Women are predisposed to certain types of sport-related musculoskeletal injuries, especially to knee-related damage. Two musculoskeletal conditions (one chronic and one acute condition) have been widely studied in female athletes. The *patellofemoral pain (PFP)* is a chronic functional disease presenting with anterior knee pain. It is caused by a dynamic malalignment of the patellofemoral joint, which is more frequent in women than in men [2]. PFP is particularly common among female runners and female athletes involved in jumping and pivoting sports (e.g. volleyball, basketball). PFP has a multifactorial origin, where quadriceps muscle function and strength, hip and core muscles strength and dysfunctional biomechanics play a role [3]. PFP is generally an exacerbating clinical condition, with multiple presentations

over the years and should be addressed promptly by the sports medicine specialist. In the presence of anterior knee pain, a rapid workout aimed at excluding all potential organic causes (i.e. patellofemoral osteoarthritis, extensor apparatus osteochondritis) should be done. Thereafter, an appropriate exercise intervention has to be implemented. A recent consensus statement indicates that a programme of strength exercises involving knee and hip muscles (in combination) is the most valuable option for treatment and prevention of PFP [4].

Women participating in pivoting, cutting and jumping sports, like soccer, basketball and volleyball, are more predisposed than men to undergo acute noncontact (without direct contact of an opponent) knee ligament injuries. For instance, the risk of a lesion of the *anterior cruciate ligament* (ACL) is 2–4 times greater in female athletes compared with male athletes with the same exposure [5]. This is particularly true for teenage soccer players, in whom the reported ACL injury rate is 11.7 per 100,000 female athletes versus 4.7 for the male counterpart [6]. The ACL injury is a serious and potentially career-threatening injury and may predispose to early onset of knee osteoarthritis. Therefore, athletic and team trainers, athletes and sports medicine doctors must be aware of such a gender-related predisposition, in order to take preventative measures addressing modifiable risk factors and decreasing the likelihood of this serious lesion.

The greater risk for female athletes of sustaining an ACL injury is related to several factors. The first one relies on the inner diversity of the musculoskeletal system, especially at the lower limb, where women present with a different static alignment, wider pelvis and greater Q angle, a narrower knee intercondylar notch and smaller ligaments [7].

The second one is due to hormonal factors. Indeed, the early ovulatory phase of the menstrual cycle is associated with the greatest risk of ACL injury [8]. On this respect, Zazulack et al. documented an impact of the menstrual cycle phase on tensile properties of the ACL, likely due to an effect of oestrogens at ACL level that has specific receptors for these hormones [9].

The third, and probably most relevant factor, is the dysfunctional neuromuscular control and biomechanical profiles shown by women during complex movement patterns. Women were found to perform cutting and landing tasks with less knee flexion, greater knee valgus and higher external knee valgus moment [10–12] that are known risk factors for ACL injuries (Fig. 12.2). A possible explanation of this motion attitude relies on a greater dominance of quadriceps muscles over hamstring and gluteus muscles in women than in men [12–14]. Consequently, women rely more on the anterior muscular kinetic chain than on the posterior one. Another aspect to be taken into account may be the static alignment of women, who generally present a wider pelvis and a greater Q angle [15]. These three biomechanical patterns place the knee ligaments at a greater risk of overload and injury. In particular, teenage female athletes should be considered “at-risk” individuals, as the increase in height and mass of the growth spurt occurring in this period of life also alters the neuromuscular control while increasing the load on static structures. The best strategy to reduce the risk of ACL injuries seems to address the neuromuscular control through specific intervention. Neuromuscular training (NMT) programmes, developed since the 1990s, consist of a series of specific exercises to complete



Fig. 12.2 Different frontal plane movement profiles of a woman and a man during a double-leg drop vertical jump. **(a)** The woman shows a bilateral *dynamic knee valgus* alignment with knee in knocked position, using the static stabilisers (bones and ligaments) to absorb ground reaction forces. This motion pattern increases the risk of knee injuries and indicates a poor neuromuscular control. **(b)** The man controls very well the leg movement, with minimum frontal plane knee motion absorbing dynamic forces through the eccentric muscles contraction

during training and before competitions [16]. Prospective trials have shown the effectiveness of these programmes, leading to a pooled reduction in ACL injuries of 73% in female sports [17]. The completion of NMT programmes at least three times a week is therefore suggested to female athletes participating in high-impact sports to reduce the risk of injury.

12.3 Iron Deficiency and Anaemia

Iron deficiency (ID) and the related anaemia are frequently encountered in young female athletes. ID prevalence in the general population of menstruating women has been reported to be up to 22% [18], but in athletes, this figure is distinctly higher, reaching 52% in adolescent athletes. It is also argued that this condition may more often occur in endurance sports (distance running) and disciplines with a high prevalence of eating disorders (gymnastics, classic dance) [18, 19]. The predisposing effect to ID of physical activity has a multifactorial origin. Any type of exercise causes a transient pro-inflammatory status, and many steps of the complex iron metabolism can be affected from this condition [20]. Secondly, an intensive exertion increases hepcidin production [20], which reduces iron absorption and disrupts its

transfer from macrophages to erythroblasts, thus favouring the development of the ID-induced anaemia. The higher rate of ID and anaemia in female compared to male athletes may be explained by the additional effect on iron loss of menses.

As a key component of haemoglobin (Hb), iron plays a crucial role in setting aerobic capacity and performance because of Hb being the main oxygen transporter to working muscles [21]. In addition, iron is a key component of the enzymatic system of the respiratory chain [20]. Hence, it is not surprising that ID adversely and greatly affects the performance and the training capacity of athletes.

ID can progress through three stages: non-anaemic ID (NAID) → ID with microcytosis and/or hypochromia (IDMH) → ID with anaemia (IDA). NAID indicates a condition characterised by a small reduction of iron store not affecting haematopoiesis. If a negative iron balance remains in place, the haematopoiesis will be affected, and the young red cells will become small and pale (microcytic and hypochromic anaemia), with a progressive reduction of mean cellular volume (MCV) and mean cellular haemoglobin (MCH). At this stage, serum ferritin is <30 mg/L, and when it crosses the threshold of 12 mg/L, also haemoglobin level starts to decrease, leading to the occurrence of the IDA. This ID evolution, frequently observed in female endurance athletes, must be distinguished from another condition that can occur in athletes, that is, the dilutional *pseudo-anaemia*, defined as low haematocrit and haemoglobin levels owing to an expanded plasma volume despite the presence of normal red cell mass and total haemoglobin mass. This condition is particularly frequent among high-level endurance athletes (prevalence of 10–15%) and can be easily distinguished for IDA as MCV and MCH remain within the normal range.

In order to prevent the development of ID during training, a regular check of blood parameters (haemoglobin level, MCV, MCH and ferritin) is warranted, especially in endurance female athletes.

When an ID is diagnosed, a proper workout is mandatory in order to exclude systemic causes (i.e. insufficient iron intake with the diet, malabsorption syndromes such as celiac disease, chronic blood loss from the gastrointestinal tract or metrorrhagia). When systemic conditions have been excluded, the first line of therapy for sport-related ID relies on *nutritional counselling*, including sufficient energy intake and five times/week intake of foods containing the haemoglobin-iron complex (i.e. fish and seafood) with the addition of legumes (i.e. breakfast cereals) and green vegetables. This should be combined with an oral iron supplementation (generally, 40–60 mg of elemental iron/day is appropriate). In order to increase the intestinal absorption, the physician should consider the use of enhancers (vitamin C) and suggest limiting the intake of inhibitors of iron uptake (coffee, black tea). In nonresponders or in the case of intolerance to oral therapy, intravenous iron supplementation should be considered. Athletes with persistently low iron values may benefit from a chronic oral supplementation, but caution should be paid as an iron overload can increase oxidative stress and induce secondary hemochromatosis (hemosiderosis). Therefore, long-term oral iron intake in the presence of normal ferritin values is not recommended and may be harmful [18].

12.4 Menstrual Cycle Irregularities

Another clinical problem of women practicing sports are menstrual cycle irregularities (MCI), especially during the early adolescence that can be prolonged in athletes, particularly in the presence of an eating disorder. As a theoretical pathological continuum, three distinct conditions of MCI have been correlated to sport: luteal phase defects, oligomenorrhoea and amenorrhoea.

Luteal phase defects (LPD) refer to a shortening of the luteal phase of the menstrual cycle, which is difficult to be diagnosed because the cycle remains regular and generally has a proper length (28 days). There seems to be a direct relationship between the amount of exercise and the likelihood of luteal phase defect development [22]. As already mentioned, LPD may precede other menstrual cycle irregularities and is related to a 2–4% bone loss per year in active sporting women [23].

Oligomenorrhoea (irregular menstrual cycle, with 3–6 menses per year) and *amenorrhoea* (absent menstruations or <3 cycle/year or no menses in the past 6 months) are more frequent in sport women than in the general female population. Their prevalence is indeed 10–20% in sport women compared to 5% of the general population, and it can be as high as 50% in competitive distance runners [24, 25]. The *primum movens* of these disorders would be an “energy drain” by physical exercise, leading to a negative energy balance. An increased energy expenditure due to strenuous and prolonged exertion, associated with suboptimal energy intake, stimulates compensatory mechanisms aimed at conserving the energy for vital functions [26]. This, in turn, causes a central suppression of reproductive function signals through the disruption of the hypothalamic-pituitary-ovarian axis which leads to a low-amplitude and irregular pulsatility of pituitary hormones and lowers the oestrogen and progesterone production. Moreover, the exercise-driven increase in corticotrophin releasing factor and corticotrophin inhibits the secretion of luteinizing hormone by the pituitary gland. Lastly, the exercise-driven increase in prolactin serum concentration may also be considered in the pathophysiology of MCI, although the exercise intensity must cross a certain threshold to cause an overproduction of this hormone [27]. The sport-related amenorrhoea is therefore a “hypothalamic amenorrhoea” and may be associated with other neuroendocrine disorders, such as thyroid dysfunction. A low fat mass is another factor which should be monitored to prevent the MCI occurrence, being both a potential risk factor (in thin athletes) for MCI development and a marker of chronic negative energy balance.

Infertility and abnormal bone mass loss (see the next paragraph) are potential consequences of MCI. As a matter of fact, fertility is generally reduced in competitive female athletes. The optimisation of both training intensity and energy intake, increasing the body fat content, is beneficial for these patients. Therefore, when a sporting woman presents with MCI, complete information on her clinical history, training volume and intensity and dietary intake should be collected. The patient must be carefully examined and her hormonal profile checked.

When the menstrual disorder is attributable to excessive exercise or an energetic imbalance, the first approach should rely on regaining a positive energetic balance by reducing the exercise volume and/or intensity and increasing/optimizing the

dietary intake in order to recover the nutritional status [28]. The same principles of optimizing nutrition and training practices should also be adopted as a preventative measure, especially in high-risk sports such as long-distance running and ballet.

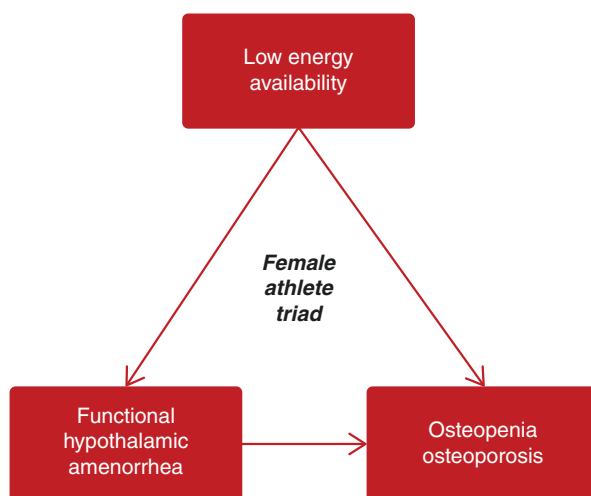
The second line of treatment, nowadays broadly utilised by athletes, is the intake of oral contraceptive pills (OCP) which can reduce both cycle irregularities and ID linked to abundant/irregular menses [29]. The prescription of this medication has to be preceded by a specific screening for cardiovascular risk factors and counseling regarding the lack of clear evidence that OCP alters performance, a frequent misconception of female athletes.

12.5 Bone Health and Osteoporosis

A correct physical exercise increases the bone mass peak and reduces the bone density loss occurring in adult and elderly people. On the contrary, an energy imbalance, due to poor nutrition and high activity output, and the consequent menstrual cycle irregularities have deleterious effects on life-long bone health, as heralded by the 4% yearly loss in bone density observed during the first 2/3 years of sport-related amenorrhoea. In order to establish a pathophysiological link between these potential problems of female athletes, the American College of Sports Medicine has proposed a triad including *low energy availability* (eating disorders and suboptimal energy intake), *hypothalamic menstrual disorder* (amenorrhoea) and *low bone mineral density* (osteopenia, osteoporosis) as interrelated factors [30] (Fig. 12.3).

The relationship between bone loss and menstrual disorders is multifactorial in nature. One cause is hypoestrogenism, but the pattern of bone remodelling in amenorrhic sporting women is atypical if compared to the postmenopausal one. Amenorrhic sporting women show *reduced* bone turnover with a reduction of bone formation [31], while postmenopausal women present with an *increased* turnover

Fig. 12.3 Female athlete pathological triad proposed by the American College of Sports Medicine



and bone resorption [32]. So, other pathogenic factors, such as a suboptimal energy intake, should be considered. Also, typical at-risk athletes, like distance runners, may have additional risk factors such as low calcium intake and greater training load [33].

Bone mass reduction in sporting women is responsible for two adverse events: (1) an increased risk of *stress fractures* during sporting or active life [34] and (2) the development of *osteoporosis* as long-term consequence.

The maintenance of the bone mass peak is crucial to prevent postmenopausal osteoporosis in former sporting women. Menstrual cycle irregularities in athletes are associated with a long-term reduction of bone mass compared with regularly menstruating athletes [35]. Proper preventative measures and treatments for the female athlete triad can annul or reduce the risk of bone mass impoverishment. Therefore, the optimisation of energy intake and expenditure, together with the intake of a well-balanced diet, should always be pursued by female athletes under the supervision of sports medicine physicians. Finally, as a low total bone mineral density (BMD) predicts stress fractures in runners [36], a pre-participation screening in female athletes at risk (i.e. long-distance runners, low-body fat athletes) may be useful to target subsequent interventions.

12.6 Conclusions

Female athletes have dysfunctional anatomical and physiological features predisposing to a number of different pathological events. The clinician should be aware of the origin and nature of these problems and should implement preventative measures consisting of exercise-based intervention, training and dietary optimisation. A proper treatment of sport-related injuries and disorders is also crucial to avoid long-term consequences.

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