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Risks, consequences and pathophysiologic pathways associated with lower limb Osteoarthritis in professional soccer athletes: a narrative review

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Abstract
The objective of this narrative review was to relate the pathophysiological knowledge of Osteoarthritis to the specific context of professional soccer, addressing the risks and consequences for athletes of the modality. The search bases used were PubMed, LILACS, Scielo, Embase and Google Scholar and the narrative review model was applied to synthesize the relevant information. Professional soccer participation exposes players to the highest frequencies and intensities of loads and joint injuries in the lower limbs. These factors are associated with greater risks of osteoarthritis development. Retired soccer athletes have a high prevalence of the disease. This scenario provides an impairment network that connects symptoms and joint limitations to the reduction in the quality of life of this population. Understanding microprocesses through the study of specific pathophysiological pathways, contribute to the evolution of monitoring, prevention and early intervention strategies for this population.

Keywords: health sports, former soccer players, joint injury, overload joint.

INTRODUCTION

Osteoarthritis (OA) is the most prevalent joint disorder worldwide with negative impacts on economic and health systems (Quicke et al, 2022). This is a chronic and progressive condition, and its etiology is multifactorial, with the involvement of genetic, systemic and biomechanical elements (Mobasheri and Batt, 2016).

The mechanical factor is essential for the development of OA, either by the direct physical factor or by the signaling cascade resulting from the

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stimulus (Vincent, 2019). In this context, the relationship between OA and sports is highlighted. Overload joint and sports-related injuries are the most commonly used arguments in the association (Tran et al., 2016; Driban et al., 2017). However, this relationship is only evident when sports are evaluated in an individualized manner (Tran et al., 2016; Driban et al., 2017). Objectively, professional level, contact dispute and change of direction are characteristics associated with the disease (Tran et al., 2016; Driban et al., 2017).

Risks of professional soccer practice to athletes' health

There is no room for generalization in discussions involving health and professional sports. In other words, high-performance sports practice should be regarded as neither a positive nor a negative factor for overall athletes' health (Kujala et al., 2003).

Metabolic, cardiovascular, neurocognitive, and musculoskeletal variables are involved and exposed to different demands in each sports practice, they interact with individual and environmental factors and promote different responses. Thus, the context of each sport and its interactions may be either beneficial or harmful depending on the health element and the moment being evaluated.

In soccer, former athletes have benefited in the long run from regular exposure to cardiorespiratory activities to prevent cardiovascular and metabolic disorders (Kujala et al., 2003; Melekoğlu et al., 2019). Nevertheless, the early specialization required by professional practice (Moseid et al., 2018) and the exposure to overload and injuries over time seems to be the price to be paid by these athletes (Turner et al., 2000; Ross, 1998; Molloy e Molloy, 2011). The persistence of these factors has an impact on the musculoskeletal system and increases the possibilities of chronic affections, especially the risk of developing OA in lower limb joints (Kujala et al., 2003; Turner et al., 2000; Ross, 1998).

Osteoarthirtis and professional soccer

Soccer is among the elite sports with a high association with the development of OA (Driban et al., 2017; Vigdorchik et al., 2017). This

occurs due to the inherent characteristics of the game and the dynamics of players' performance that lead to maximum joint demands: high impact and intensity of practice, physical contact, use of rotational loads, and high rates of joint injuries (Lee e Chu, 2012). It is believed that OA affects approximately 32 to 49% of former professional soccer athletes (Krajnc et al., 2010; Kujala et al., 1994), especially in lower limb joints – hip (Vigdorchik et al., 2017), knee, and ankle (Kuijt et al., 2012).

The official health analyses of the International Federation of Football (FIFA) emphasize the concern with the healthy aging of this population (Mandelbaum et al., 2012) and highlight the degenerative joint problems in athletes (Dvorak e Junge, 2015). The most recent annual update on biological aspects related to OA points to the need to focus efforts on understanding the pathophysiological processes related to the disease (Jiang, 2022).

Nonetheless, literature discussing the processes involved in the underlying disease genesis applied to the soccer context is scarce. Understanding the pathophysiological mechanisms that are associated with the sport's dynamics allows structuring the basis for discussions on the subject and evolving prevention and early intervention strategies in this population.

Based on this, the objective of this study is to synthesize the pathophysiological knowledge available in the literature and connect it to the characteristics of soccer. This content in narrative review format is focused on providing a dynamic and integrated reading on the topic, which can serve as a basis for future studies in this line of research.

METHODS

The databases used in this research were PubMed, LILACS, Scielo, Embase and Google Scholar. The selected studies were published in English and no time limit was used in the search. The keywords used were strategically grouped to better contemplate each topic, namely: soccer, osteoarthritis, lower limbs, hip injuries, knee injuries, ankle injuries, joint injuries, joint demands, physiopathology and pathogenesis of osteoarthritis.

RESULTS

Overview of pathophysiologic processes in OA

All joint components are involved in the setting of OA: subchondral bone, synovium, ligaments, capsule and articular cartilage contribute to and are affected by the pathophysiological processes of the disease; muscles, nerves, bursae and fat pads express modifications and impairments as a result of previous alterations of the other joint elements (Loeser et al., 2012). Despite the entire joint complex's participation, cartilage involvement is the main disease characteristic, due to the important physiological and biomechanical roles of this tissue (He et al., 2020).

The definition of OA by the Osteoarthritis Research Society International (OARSI) depicts the molecular derangement expressed during the early stages of the disease as the trigger for the cycle of unsuccessful repair responses, i.e., the pathogenic process starts due to homeostatic impairment of joint tissues caused by cellular imbalance (OARSI).

In an attempt to reestablish homeostasis, regardless of initial imbalance causing factors, chondrocytes increase their extracellular matrix (ECM) synthesis and proliferation activities, which sets up the anabolic compensation period (Mobasheri et al., 2017) and results in the initial biochemical and oxidative stress (Rim et al., 2020). Another important step in the process is the hypertrophic differentiation and chondrocyte senescence. These phenomena compromise cellular functionality and fuel the next stages of the pathophysiological process (Rim et al., 2020). With this setting, there is an exacerbated production of inflammatory proteins (mainly interleukins 1 and 6) and degradative enzymes (metalloproteinases and disintegrins) (Nguyen et al., 2017), a phenomenon that attracts and activates the innate immune system through the recognition of toll-like receptors, which are already present in large quantities in chondrocytes and activated in cell destruction situations71. Inflammatory and degrading elements are intensified by immunological action and make the catabolic process superior to local anabolic capacities (Molnar et al., 2021).

Other joint components are also important contributors to pathogenic actions. Both subchondral bone and synovial membrane contribute in the release of inflammatory cytokines and degradative enzymes; these tissues undergo processes of hypertrophy and hyperplasia of their specialized cells (Glyn-Jones et al., 2015). Another characteristic of the

disease, the maintenance of the inflammatory process is influenced by the release of degradative fragments into the synovial fluid, which allows the constant reactivation of the local inflammatory process – synovitis (Berenbaum, 2013).

The resulting phenomena of cell apoptosis, chondral fibrillation and erosion, invasive neovascularization, and calcification of the articular cartilage make it unfeasible for the cartilaginous tissue to be fully functional (Rim et al., 2020). Insufficient regulatory pathways (OARSI) add to previously described processes, which, occurring cyclically and dynamically, characterize OA (Nguyen et al., 2017).

Pathogenic pathways associated to lower limb OA in soccer athletes

The contribution of soccer demands and characteristics to OA can be segmented into two main pathophysiological pathways: the post-traumatic one, resulting from joint injuries and their consequences, and the chronic overload one, originating from the maintenance of high joint demands over time.

Post-traumatic pathway

Joint injuries in the lower limbs are typically high in soccer. Regarding prevalence, knee, ankle and hip injuries are second only to thigh muscle injuries (López-Valenciano et al., 2019). These characteristics are important contributors to risk for the genesis of OA, with approximately 12% of all cases of the disease being post-traumatic (Jiménez et al., 2018).

Traumas affecting chondral tissue are common in sports like soccer. The most accepted theory, obtained in vitro analyses, is that the impact provided by trauma stimulates the release of oxygen free radicals from the mitochondrial electron transport chains of the chondrocytes, and this phenomenon triggers changes in local homeostasis (Martin et al., 2009). This event may lead to death in directly affected cells and provide metabolic modifications in surviving ones, which limits their tolerance to mechanical loads and induces the weakening and rupture of matrix components (Vincent, 2019).

Increases in the expression of pro-inflammatory and degradative signaling, such as interleukin-1 and matrix metalloproteinases, are also post-traumatic consequences and configure the initial pathophysiological

setting, with the potential for evolution in the cascades of reactions (Guilak et al., 2004).

In acute periods, chondrocyte apoptosis is an important signaling factor due to its irreversibility characteristic, a phenomenon that occurs between 6 hours and 7 days after injury (D'Lima et al., 2001). Within 3 days after injury, there is also evidence of reduced proteoglycan synthesis (D'Lima et al., 2001), followed by changes in joint collagen levels that show a downward surge within one-month post-injury (Catterall et al., 2010).

The amount of energy involved in the injury mechanism contributes to different tissue responses. Common injuries in professional soccer athletes are capable of generating structural and physiological modifications in joint components and contribute to the process of joint degeneration. Anderson et al (2011), found that low traumatic energy does not result in macroscopic injury, but has physiological effects on cellular and matrix components, while higher energy levels affect joint surface elements both micro-and macroscopically.

Injuries to joint tissues other than cartilage, such as fractures, sprains, ligament, and meniscal injuries also influence the genesis and progression of local degenerative processes, as they modify joint structures and mechanics through changes in the load incidence vectors and, consequently, the contact areas on the joint surfaces (Buckwalter et al., 2013). This exposure to compressive and shear loads in unusual regions alters local cartilage homeostasis and may lead to cell death mechanisms and matrix deletion that may result in chondral injury and/or degenerative processes (Buckwalter, 2003). Regardless of the joint, even after surgical reconstructive approaches, 20 to 50% of cases may progress to post-traumatic OA (Anderson et al., 2011).

Chronic overload pathway

Imposed loads regulate joint metabolism and are critical for maintaining the processes of inflammatory suppression and degradative control of chondral componentes (Sun, 2010). There is evidence that moderate physical activity (Lequesne et al., 1997) and joint loads from daily activities do not increase the risk of developing lower limb OA (Arokoski et al., 2000). However, high joint demand may exceed self-regulatory benefits and contribute to local catabolic predominance (Guilak, 2011).

Soccer practice exposes lower limb joints to different loads and alignment conditions due to its basic moves - acceleration, deceleration, changes of direction, jumps, and kicks - associated to the dispute involving physical contact with opponents. This provides an unpredictable range of levels and directions of loads on the athletes' hip, knee, and ankle joints. Professional participation increases the frequency and intensity of these exposures and is therefore associated with an increased risk of OA compared to the general population (Kuijt et al., 2012; Molloy e Molloy, 2011; Gouttebarge et al., 2015).

The joint mechanical environment influences the expression of mechanosensitive genes capable of acting on matrix components and controlling cartilage growth or degradation factors over time (Carter et al., 2004). Joint overload contributes to an important pathophysiological feature of degenerative processes: the expression of pro-inflammatory mediators and cytokines, such as nitric oxide and interleukin 1β (He et al, 2020).

Pro-inflammatory cytokines have the ability to reactivate chemokines and perpetuate the maintenance of the low-grade inflammatory process. This is an important feature of the pathophysiological process, as it becomes the main source of stimulus for the action of catabolic enzymes, metalloproteinases and disintegrins, and a focus of attraction for inflammatory cells (Molnar et al., 2021).

Not all the mechanisms and possibilities of interaction of the mechanobiological pathways have been fully understood yet, however, chronic maintenance of these conditions makes chondrocyte repair actions and cartilage functionality unfeasible, and this seems to be the basic mechanism that associates the maintenance of joint overloads with OA genesis.

DISCUSSION

Soccer-specific joint injuries and loads: risks and association with pathophysiological pathways of OA

Hip joint

The most prevalent hip joint injuries in soccer athletes are femoroacetabular impingement (FAI), acetabular labrum injuries, and articular cartilage injuries (Di Pietto et al., 2018; Sherman et al., 2018).

High-impact sports such as soccer, played by individuals continuously and at high intensity during the growth phase, may influence the onset of FAI (Vigdorchik et al., 2017; Agricola et al., 2012). This condition is present in 72% of the athletes (Gerhardt et al., 2012). Exposure to sports practices generates local microtrauma as a result of contact changes in the joint elements, which can result in chondral and labral lesions, predisposing to hip osteoarthritis (hip OA) (Ganz et al., 2003).

The first evidence on the association between hip OA and playing soccer was weak (Solonen, 1966). Years later, studies began to suggest the presence of this relationship in professional athletes. Researchers systematically evaluated clinical and radiographic signs in former soccer athletes and non-athlete controls and identified that approximately 49% of former athletes had positive signs of hip AO (Klunder et al., 1980). In the early 2000s, more studies found similar results (Turner et al., 2000; Shepard et al., 2003).

Although the prevalence of hip OA was higher in former soccer athletes than in the general population, the contribution of prior injury did not seem to have as much impact, since the involvement history in this joint was not as significant as in the other lower limb joints (Shepard et al., 2003). The level and type of joint demand became important factors to be investigated. It was identified that athletes in high-impact sports practiced at a professional level, such as soccer, were at high risk of developing hip OA, but professional long-distance runners were not at clear risk of association with the disease (Vigdorchik et al., 2017). These data indicate that sport specificities require distinct forms of joint demands and lead to different outcomes. For example, soccer practice exposes the hip joint to frequent rotational loads, high intensity, and little predictability of action, which are opposite to long-distance running practice with strictly cyclical and linear demands.

The most recent review on hip OA associated with soccer demonstrated higher prevalence rate in former athletes, this being 8.6%, and 5.6% in non-athletes (Petrillo et al., 2018). Radiographic prevalence rates also remain higher in the former athletes' group, 21.2% and 9.8%, respectively (Petrillo et al., 2018).

In turn, Hall et al (2021), synthesized the most current differences in the pathophysiological processes of the hip and highlighted the positive

relationship between pain in hip OA and levels of concentration of inflammatory cytokines, such as interleukin-6. It is also notorious, the potential influence of collagen VI protein regulatory gene expression on the rate of disease development, lower gene and protein expression appears to accelerate hip OA with aging (Hall et al., 2022). These contributions highlight the complexity of the interactions that result in the expression of the disease and the challenge of understanding them in the long term.

Despite that, evidence supports that soccer practice at a professional level is associated with the development of hip OA, especially regarding continuous lower limb joint overload. It is necessary that the discussion concerning this relationship considers joint morphoanatomical specificities and biomechanical demands practice in order to understand the pathophysiologic processes and the real influences of soccer context on joint health.

Knee joint

The earliest evidence expressed no significant differences in the prevalence of knee osteoarthritis (knee OA) when comparing former soccer athletes and control subjects (Solonen, 1966; Klunder et al., 1980). In 1985, for the first time, higher radiological signs of knee OA were observed in former soccer athletes (Chantraine, 1985). According to the authors, this factor could be explained by the number of joint injuries and altered varus knee alignment identified in the athlete population (Chantraine, 1985). Cross-sectional studies in the 1990s and early 2000s confirmed a higher prevalence of knee OA in professional athletes and highlighting the association with typical injuries of the sport (Roos et al., 1994; Kujala et al., 1995; Larsen et al., 1999; von Porat et al., 2004).

The most common knee joint injuries in soccer athletes are anterior cruciate

ligament (ACL) injuries; meniscus; cartilage and other ligaments. ACL injuries have the highest prevalence, with annual values ranging from 0.6 to 8.5% (Waldén et al., 2011). A high prevalence of knee OA was identified in former soccer athletes after 14 years of ACL rupture: 78% of the participants showed radiographic changes in the injured joint, 41% with signs of moderate knee OA (von Porat et al., 2004). In this same analysis, approximately 38% of ACL ruptures were associated with

meniscal lesions, and of these, 59% evolved to radiographic changes compatible with moderate and advanced levels of the disease (von Porat et al., 2004).

The function of joint stabilization provided by knee ligaments is fundamental in the discussion on the relationship between injuries and OA. Other than ACL, knee ligament injuries are scarcer in soccer athletes, but they also directly contribute to the length of absence and health variables of athletes, for instance, the need for joint surgery (Waldén et al., 2011).

Cartilage involvement is also common and is usually associated with injuries of other structures from the joint complex. The mapping of knee cartilage lesions shows that 51% of the disorders occur in the medial femoral condyle, 27% in the lateral femoral condyle, 10% in the trochlea, 8% in the patella and 4% in the tibial plateaus (Andrade et al., 2016). As well as isolated ligament and meniscus injuries, chondral involvement can also be a major contributor to knee degenerative processes (Buckwalter e Mankin, 1998). Trauma-related alterations and changes in intra-articular load incidence after injury seem to contribute to a cascade of pathophysiological reactions and to the onset of knee OA (Lohmander et al., 2007).

The latest updates on the pathophysiological mechanism of OA in the tibiofemoral joint demonstrate the important influence of the subchondral bone remodeling process on the onset and evolution of the disease. More precisely, through this process, vascular channels are installed that allow communication between bone and cartilage and, consequently, alter the biochemical interaction of chondrocytes. This change in homeostasis affects the maintenance of the local catabolic process and, as it is structurally associated with the neogenesis of nerve endings, it may also be one of the reasons that explain the pain in tibiofemoral AO (Jang et al., 2021).

Prevalence data of knee OA in former soccer athletes range from 60 (Elleuch et al., 2008) to 80% (Krajnc et al., 2010) and diverge on methodological issues of injury and OA diagnostic classification. At any rate, the influence of intra-articular injuries, mainly ACL and meniscus, seems to contribute to the disease development in this population. Nevertheless, the high lower limb joint demands and soccer

biomechanical specificities should also be considered and further studied, in order to truly assess the relationship between knee OA and soccer.

Ankle joint

The main ankle injuries in soccer athletes are ligamentous involvement, fractures and osteochondral lesions and anterior and posterior ankle impingement (Nery et al., 2016). Among all the injuries of this joint, 80% are caused by sprains (Fong et al., 2007).

The most common sprains are caused by inversion and may lead to ligament injuries in the lateral ankle complex (Hintermann, 1999). The injury's mechanical action may distend other local soft tissues, such as the joint capsule, which compromises local proprioceptive components and contributes to chronic instability of this joint, which may cause injuries to other ankle structures over time (Hubbard-Turner, 2012). It is estimated that 78% of these cases may evolve to ankle osteoarthritis (ankle OA) (Harrington, 1979).

Sprains having a higher degree of injury may not only affect ligaments but also osteochondral components, being the talus medial osteochondral region twice as affected as the lateral one, and the central one more affected than the anterior and posterior regions (Elias et al., 2007). This degree of involvement may also lead to ankle fractures, and although they are less prevalent in overall injury findings of this population, this kind of injury is the most predominant among all lower limb fractures (Dvorak and Junge, 2000). The presence of joint fractures is associated with cartilage damage and the development of ankle OA (Stufkens et al., 2010).

Repetitive microtrauma injuries, inherent to high joint demand, are also present in soccer athletes and are associated with OA risk, the most common being anterior and posterior ankle impingement (Nery et al., 2016).

Anterior impingement is associated with repeated trauma and traction of the ankle anterior capsule, a common mechanism in the contact between the foot and the ball in the kicking gesture (Tol and van Dijk, 2004). McMurray (1950) described this as "footballer's ankle" due to its high prevalence in soccer athletes and its relationship to local pain in this population (McMurray, 1950), approximately 60% (Valderrabano et al., 2014). Posterior impingement is also commonly reported in this

population and may have its origin associated with local fractures or soft tissue involvement (Hedrick and McBryde, 1994).

Identifying changes consistent with ankle OA in former soccer athletes has been documented since the earliest investigations of the topic in the literature (Solonen, 1966; Brodelius, 1961). Acquired local instability and joint incongruity result in abnormalities in load incidence and appear to be important mechanical risk contributors to the development of ankle AO (Delco et al., 2017). Current evidence supports a relationship between prior joint injuries and ankle OA in soccer athletes, approximately 70% of cases are post-traumatic in nature, mainly in sprains with resulting ligament injuries and/or fractures (Valderrabano et al., 2014). The disease prevalence in this joint ranges from 9.2 (Paget et al., 2020) to 17% (Turner et al., 2000; Drawer and Fuller, 2001), values higher than those found in the general population, 3.4% (Murray et al., 2018).

Updated conclusions on the pathophysiological process involved in ankle OA demonstrate that the main factors related to the evolution of the condition are: low cartilage repair capacity after direct trauma and a broad and long-lasting inflammatory process in the synovium, with maintenance of high rates of cytokine expression inflammation for up to 6 months after injury (Godoy-Santos et al., 2020).

Nevertheless, the average latency time between lesions of ankle joint components and the onset of OA in this joint can reach 34.3 years (Valderrabano et al., 2006). This time and the individual interactions for the predisposition of the clinical picture are major challenges in mapping possible OA presentations, especially in professional athletes.

Consequences and impacts of OA on former soccer athletes

As presented throughout this discussion, the context and objectives present in professional-level sports activities may exceed the already known benefits of physical activities and negatively impact the musculoskeletal system. Soccer, a sport with a great popular and economic appeal, has a setting of players living with pain, injuries, surgeries, accelerated rehabilitation, and high training and competition intensity which makes it very difficult to distinguish what is normal from

what is harmful to active athletes. The consequences are usually widely reported in the post-career period, and the evidence follows this trend.

Fujii et al (2022) point out that the aging process itself is a major risk factor for OA. Over time, chondrocytes enter senescence processes and this phenomenon results in two harmful characteristics: reduced capacity for oxidative stress and impaired cell survival function through autophagy (Fujii et al., 2022). That is, aging can also effectively contribute to the pathophysiological process of OA.

Former athletes have a high propensity to develop lower limb joint pain, especially in the knee and ankle (Drawer and Fuller, 2001), and more than 17% of reports of pain in these joints are due to OA (Gouttebarge et al., 2014). Gouttebarge et al (2015) point out that 90% of this population report moderate and severe levels of joint pain and approximately 65% experience daily living mobility and performance restrictions.

Symptom persistence associated with insufficient conservative therapeutic interventions, such as physical therapy treatment and body mass index control, culminates in arthroplasty and presence of health comorbidities (Gouttebarge et al., 2014). Lohkamp et al (2017) found that the number of hip arthroplasties is higher in former professional soccer athletes than in the general population. As for the knee and ankle joints, this difference also exists, but it is smaller and with an only moderate level of evidence in the literature (Lohkamp et al., 2017).

Pain, mobility restriction, daily activities impairment and the need of arthroplasties reflect on psychosocial aspects: 37% of former athletes reported symptoms of depression and/or anxiety (Gouttebarge et al., 2015). The combination of this physical and psychosocial picture results in reduced quality of life. When compared to non-athlete controls, former soccer athletes express lower scores on the Short Form Health Survey 36 (SF-36 Questionnaire), which indicates a worse perception of quality of life, with physical complaints, pain, and joint symptoms contributing significantly to this Picture (Arliani et al., 2014).

Professional soccer athletes' careers are marked by their brevity and high-intensity level; these features evidence musculoskeletal damages in retirement, especially in OA cases, which may evolve to persistent physical symptoms and negative consequences in psychological and social aspects.

CONCLUSION

Evidence suggests that high joint demand, especially in the hip, and greater exposure to joint injuries, especially in the knee and ankle, contribute to the high rate of lower limb OA in soccer athletes.

The level of professional performance and the innate characteristics of the practice make joint demands an immutable factor in this context. On the other hand, preventing joint damage adds performance benefits and minimizes the risk of future damage such as OA. Therefore, the application of joint injury prevention programs that are based on multifactorial monitoring models during the professional career can be considered a viable practical strategy. Due to the characteristics of the disease and the population profile, the incentive to maintain health care after retirement can also be seen as a tool to reduce risks and damages in the long term.

In the scientific field, we emphasize the need for more studies with tools that can measure early changes in joint health and contribute to the refinement of early intervention strategies applied to the modality.

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