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The role of classical risk factors for knee osteoarthritis in unilateral transtibial amputation

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Abstract

The study aimed to review the literature on the classical risk factors for knee osteoarthritis and their possible role in the development of this pathology in patients with unilateral transtibial amputation in terms of potential rehabilitation prospects. A search of publications was carried out using PubMed databases of the US National Center for Biotechnology Information and the website of the Elsevier publishing house. Well-established increased risk factors for knee osteoarthritis are old age, female gender, lower limb muscle weakness, low or excessive physical activity, overweight, a history of knee joint injury or surgery, chronic knee pain. These factors are common for disabled persons with unilateral transtibial amputation, which, combined with specific mechanical factors, makes these persons more vulnerable to the development and progression of osteoarthritis. Programs aimed at eliminating modifiable risk factors for the development of knee osteoarthritis can contribute to the preservation of knee joint function in the long term and improve the quality of life of persons with unilateral transtibial amputation. This requires the well-coordinated efforts of a multidisciplinary team, as well as the participation of the disabled persons themselves. Identification and management of the potentially modifiable classical risk factors for the development of knee osteoarthritis are one of the promising pathways of rehabilitation of persons with unilateral transtibial amputation.

Keywords: knee osteoarthritis, risk factors, lower limb loss, unilateral transtibial amputation, rehabilitation.

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Introduction. Osteoarthritis (OA) is a multifactorial condition of articular insufficiency characterized by the loss of articular cartilage, sclerosis of the subchondral bone, and inflammation leading to progressive joint degradation, structural changes, loss of mobility and function, pain, and low quality of life [1, 2]. OA of the knee joint progresses slowly; however, X-ray diagnosis is often made only at a late disease stage [3]. Given the degenerative nature of knee OA, it usually progresses to a stage where joint replacement surgery may be the only option to relieve symptoms and improve function and quality of life. However, this procedure may be unacceptable for patients with transtibial amputation [4].

For this reason, identifying potentially modifiable risk factors and implementing protective strategies that can lead to favorable long-term results are necessary. Currently, lifestyle changes, physiotherapy, physical exercise, and other methods of physical and rehabilitation medicine are main methods that slow OA progression [5].

Individuals with unilateral transtibial amputation are known to have an increased prevalence of OA and pain in the knee joint of an intact limb [6, 7], which is associated with impaired gait biomechanics and a compensatory load increase on this joint [8]. Moreover, classical risk factors for the development of knee OA received insufficient attention.

This study aimed to analyze the literature on the classic risk factors for knee OA and their possible role in the development of this pathology in people with unilateral transtibial amputation from the perspective of potential rehabilitation prospects.

Materials and methods. Relevant studies were extracted from the PubMed databases of the US National Center for Biotechnology Information on the Elsevier website using the keywords “knee osteoarthritis,” “knee pain,” “risk factors,” “lower-limb amputation,” “transtibial amputation,” “below-knee amputation,” and “satisfaction.” Full-text articles relevant to the study problem were analyzed. During the search for the most appropriate

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publications, "similar articles" recommended directly on the indicated sites were extracted.

Results and discussion. The commonly recognized factors that contribute to an increased risk of developing knee OA in the general population are an overweight status, presence of clinical symptoms (primarily pain) without X-ray confirmation of OA, history of knee injury, or history of knee surgery [9]. The highest prevalence of knee pain and OA was noted in elderly people and women [10]. Genetic predisposition is of no small importance in OA development; however, at present, genetic predisposition is difficult to assess clinically [11].

The risk factors for OA of the knee joints also include increased load on the joints [12], physical activity, and muscle weakness [13].

The relevance of risk factors for the development of OA for the population with unilateral transtibial amputation appears to be more significant than that for other population groups.

Age. Elderly age is a well-known risk factor for OA occurrence. The relationship between age and OA risk is believed to be multifactorial. It can be caused by metabolic disorders with an intensification of oxidative processes, changes in cartilage structure, a decrease in muscle strength with sarcopenia development, and a decrease in proprioception [14]. Age-related changes in cellular mechanisms that maintain homeostasis also contribute to an inadequate response to stress and destruction of articular tissues [15].

If we consider the population of amputees in developed countries, most of them are over 60 years old [16]. This population is vulnerable to the development and/or progression of knee OA, which must be considered when drawing up rehabilitation programs and prosthetics.

Gender. An opinion is expressed about gender differences in the pathogenesis of OA [17], which is associated apparently with the status of sex hormones, especially with the estrogen level. This is evidenced by the data on the higher prevalence of OA in women [18, 19], increase in OA prevalence among postmenopausal women [20], and presence of estrogen receptors in the tissues of the joints [21]. An experimental study on mice demonstrated that estrogen plays a protective role in maintaining joint homeostasis, preventing damage to cartilage and changes in the subchondral bone of the joints [22]. A study did not find gender differences in the frequency of major lower-limb amputations [23]. However, female patients were older at the time of amputation [24]. From these perspectives, the gender dependence of knee OA is also relevant for female patients with transtibial amputation.

Overweight. Obesity is one of the proven modifiable risk factors for knee OA. According to Murphy et al., two of every three patients with obesity have OA [25]. Zhou showed the dependence of OA development on body mass index [26].

Obesity is believed to be associated with both the development and progression of knee OA [27]. Conversely, weight loss of more than 5% in people with risk factors or radiographic signs of OA has been shown to be associated with slow progression over 96 months of knee cartilage degeneration and slow progression of meniscus lesion compared with study participants with stable weight [28].

Despite the proven relationship between obesity and OA development, there is serious debate about how obesity contributes to the disease onset and progression. A combination of increased load and altered joint biomechanics is considered the main mechanism of the relationship between obesity and OA for load-bearing joints [29]. Moreover, because of the anatomical aspects, obesity affects to a greater extent the induction and progression of OA in the knee joint than in the hip joint [30].

According to Chen et al., abnormal load in obesity plays a central role, while joint displacement and muscle weakness have a dynamic relationship, influencing each other and exacerbating the effect of abnormal load on the joints [30]. Muscle hypotrophy in obese people limits the full functioning of the joints, contributing to their displacement. The combination of these three factors affects the structure of the joints, stimulating OA onset and progression [30].

A sedentary lifestyle increased the risk of people with disability associated with lower-limb amputation to experience weight gain and obesity. According to Littman et al., only 23% of patients with lower-limb amputation had normal weight, one-third were overweight, and 26% and 17% had obesity I and II, respectively [31], which leads to an increased risk of knee OA.

Literature data indicate the importance of including measures to maintain normal body weight or reduce it, if necessary, in the rehabilitation program for people with disability associated with transtibial amputation to prevent the development and/or progression of knee OA after prosthetics.

Muscle weakness. Patients with OA usually develop impaired muscle function, including weakness, with changes in the sequence, degree, and rate of activation because of impaired neuromuscular transmission mechanisms and proprioceptive deficits [32]. The muscles of the elderly population are more susceptible to damage and regenerate and recover more slowly than the muscles of the young population. They also become atrophic and weak more often.

Muscle weakness was previously considered a secondary sign because of OA-related symptoms that lead to decreased activity levels with subsequent muscle hypotrophy and weakness. However, muscle weakness precedes the onset of knee OA [33]. This is especially relevant for the extensors and flexors of the knee [34]. The loss of strength of the quadriceps can reduce its shock-absorbing potential, causing large dynamic loads on the knee joint cartilage and subsequent progressive cartilage degeneration [32, 35, 36].

A study suggested that weakness of muscles involved in hip joint movement may also contribute to an increased risk of knee OA [37]. In particular, this concerns the thigh muscles, which are involved in the alignment of the frontal and horizontal planes of the lower extremities [37]. Strengthening the abductor muscles of the thigh can lead to a significant reduction in pain and improved functioning in older people with primary OA of the knee joint [38].

Patients with lower-limb amputation experience acute muscle weakness. In the absence of plantar flexors, the knee and hip extensors become more important for movement. However, a study revealed evidence of muscle changes during transtibial amputation, i.e., a decrease in the strength of the extensors (quadriceps) and knee flexors [39]. Decreased strength of the quadriceps can impair the ability of the prosthetic limb to perform adequate movement [40]. Considering the predominantly old age of people with disability associated with lower-limb amputation, muscle weakness is an urgent problem.

According to Esposito and Miller, a decrease in strength in the preserved muscles of the stump may increase metabolic consumptions during walking in patients with unilateral transtibial amputation [41]. The authors believe that minimizing muscle strength reduction, especially in the prosthetic limb, should be the focus of rehabilitation after transtibial amputation to maintain low-energy walking with minimal gait deviations [41]. Nolan also emphasized the need to maintain the stump muscle strength and muscle strength symmetry between the limbs [42]. According to Zhang et al., during rehabilitation training, weight loss and increase in muscle mass, should be given special attention, as they may have reduce the risk of knee OA in this population [43].

Lefèvre-Colau et al. believe that rehabilitation strategies to improve long-term muscle function in patients with OA should include appropriate exercise and physical activity [44]. Muscle-strengthening exercises have been shown to reduce pain and improve physical functioning and quality of life of patients with knee OA; however, these benefits usually do not persist after the patient stops exercising [45]. This indicates the need to inform people with disability about the importance of regular physical exercise and learning how to do it independently at home.

Physical activity level. Data on the effect of physical activity on OA development and progression are conflicting, which may be attributed to some research limitations. For example, the authors may not have considered the additional role of trauma obtained during exercise. Moreover, knee structures may behave differently when performing diverse physical activities at various stages of life [46].

The intensity of physical activity appears significant. In particular, a study revealed that sedentary lifestyle and vigorous activity may be unsafe for people at risk of developing knee OA [46] and that both low and excessive physical activities are accompanied by cartilage degradation [47, 48]. An increased risk of knee OA was noted in male patients who were overweight and obese and had increased physical activity [49]. On the contrary, a study revealed that less active middle-aged people may also develop knee OA [50].

Nagao et al. believe that extremely intense sports increase the OA risk, while daily exercise reduces it [51]. Other authors also indicate a reduction in OA risk with regular physical activity throughout life [52]. This may be due to a decrease in the action of some other risk factors for the development of knee OA (such as a decrease in quadriceps strength) [53].

Moreover, the reduction in the risk of knee OA with regular physical activity is explained by "conditioning" of the cartilage [54]. In this theory, the cartilage can adapt to stress, and prolonged periods of low activity followed by short periods of intense activity can destroy cartilage and increase the risk of OA.

Intra-articular cartilage is positively affected by various physical exercises [55, 56]. In addition, exercises do not negatively affect the biochemical composition of the articular cartilage of the knee joint in the population with mild knee OA and are well tolerated [55, 56].

Moderate physical activity is recommended by the guidelines for the nonsurgical management of knee OA [57].

Considering the above, people with unilateral transtibial amputation appear to have an increased risk of knee OA because of low physical activity level [58].

Miller et al. explained that the increased risk of knee OA in people with unilateral transtibial amputation is related to cartilage "conditioning," i.e., abrupt changes in gait mechanics because of

amputation and the use of prostheses lead to a sudden increase in the load on the joints of the intact limb, in which the adaptive response of the cartilage was weakened by a long unloading period because of trauma and/or surgery [59].

Articular cartilage is thought to undergo some degrees of structural and functional atrophy in the absence of mechanical stress. In particular, the glycosaminoglycan content in the cartilage of the knee joint, which affects the stiffness of the cartilage during compression, remains below the initial level for at least 1 year after 6 weeks of immobilization [59]. Thus, excessive load on the intact limb after immobilization may be dangerous for the knee joint condition in the future. To minimize this risk, long loading periods of axial load should be avoided [59].

At present, it remains unclear whether sports can be a risk factor for the onset and progression of knee OA in patients with lower-limb amputation [7]. However, a study revealed that people with disabilities associated with a post-amputation defect of the lower limb, who are involved in sports and/or are physically active, report significant physical and psychological improvements (i.e., increased strength, endurance, and self-esteem and quality of life) [60].

Knee injury or surgery. Joint injury is considered one of the most serious risk factors for OA development [61]. Studies have shown that people with a history of knee injuries have a significantly higher risk of knee OA [24] and their diagnosis is established earlier [62].

In contrast to idiopathic OA, post-traumatic OA can cause functional disability in disproportionately young populations, as primary injuries are more likely to occur in young people [63]. Moreover, injuries of the anterior cruciate ligament are dominant, especially in young people involved in sports that require turns and frequent direction changes [63]. According to various sources, 50%–90% of injuries of the anterior cruciate ligament progress to OA [64, 65]. In turn, anterior cruciate ligament injury can cause pain, limited range of motion, muscle weakness, knee instability, altered biomechanics, and decreased physical activity [65], determining a secondary risk of knee OA.

Several other factors may mediate the risk of post-traumatic OA, namely, female gender, age, high body mass index, obesity, physical activity, smoking, low educational level, subsequent surgery, surgical intervention, and knee varus alignment [64, 66].

The exact mechanism of development of post-traumatic OA remains unclear. Structural, biological, mechanical, and neuromuscular factors are believed to be involved in this process [67].

After a knee injury, there may be an "early therapeutic window" during which the inflammatory response is activated and matrix degradation starts, which can be targeted by intervention; however, the optimal and/or most recent times at which degradation can be stopped or reversed are currently unknown [68].

Physical activity is considered important in the rehabilitation of patients with post-traumatic OA. According to Dare and Rodeo, since the joint range of motion is often limited in case of post-traumatic OA, the main emphasis should be on normalizing the range of motion and strength training of the quadriceps and popliteal tendons [69].

Some authors highlight the importance of informing patients about rehabilitation for post-traumatic OA, as it is necessary to increase their awareness of the possibility of repeated injury and risk of post-traumatic OA, helping them to understand the importance of preventing repeated injury and training them to engage in physical activity, control of weight, and diet [70].

Post-traumatic OA may be relevant for patients with disability associated with transtibial amputation due to trauma. Serious injuries of the lower extremities requiring amputation are becoming an increasingly common problem for military and civilian surgeons and trauma orthopedists [71]. The predominance of men and young people (average, 37.2 years) with limbs amputated because of traumatic injury is an important finding [72].

Patients with traumatic unilateral lower-limb amputation are at a higher risk of OA of the contralateral knee joint compared with people without amputation [4, 73].

The high life expectancy of young people with trauma suggests the development of effective rehabilitation programs to prevent or delay the development of knee OA by early identification and modification of risk factors. Rehabilitation programs should include screening of an intact limb for previous high-energy trauma, assessment of joint pain, evaluation of biomechanics of the contralateral knee joint, and should aimed, among other things, at managing body weight and eliminating muscle weakness in the lower extremities [4].

Chronic knee pain. The presence of chronic knee pain is considered an early sign of degenerative joint changes that may appear prior to radiographic signs of knee OA, since the most commonly used conventional radiographs are not sensitive to detecting early structural changes in OA [74].

The intensity of knee pain was reported to be a predictor of total knee replacement in OA [75]. Thus, pain relief through inexpensive and non-invasive treatment methods is of interest. These methods

include gait aids, gait biomechanics correction, specific physical exercises, and joint fixation [9, 57].

According to Norvell et al., in patients with transtibial amputation, pain in the knee of the intact limb occurs nearly two times more often than in the control population and five times less often in the knee of the amputated limb [76]. Complaints of pain in the contralateral knee joint are more common in women (37%) than in men (24.1%) [77]. If we take into account the earlier opinion that the chronic knee pain is an early sign of the knee OA [74], then it is probable that measures aimed at reducing pain (or preventing it) will delay (or prevent) the clinical and radiological manifestation of OA in patients with transtibial amputation.

Conclusion. The knee joint has a unique load-carrying mechanism that can withstand normal daily loads without injury, which is determined by genetic, mechanical, and age-related factors. However, the effect of excessive loads and changes in the biomechanics of the joints following lower-limb amputation, in combination with other risk factors characteristic of people with disability with unilateral transtibial amputation (usually elderly patients or traumatic etiology of limb amputation at a young age, decreased physical activity, muscle weakness, and overweight) can lead to the onset and progression of OA.

The development of effective rehabilitation programs to prevent or delay OA of the knee joint by early detection and modification of risk factors is believed to be a decisive step in maintaining knee function in the long term and improving the quality of life of people with disabilities after unilateral lower-limb amputation [4]. This requires the well-coordinated work of a team of doctors, prosthetists, physiotherapists, and other specialists and the participation of the patients [78, 79].

CONCLUSIONS

1. The main generally recognized classical risk factors for the development of OA of the knee joint are old age, female gender, overweight (obesity), weakness of lower-limb muscles, low or excessive physical activity, history of injury or surgery of the knee joint, as well as chronic knee pain.

2. People with disability associated with unilateral transtibial amputation of a limb is characterized by a high frequency of the following factors: age >60 years, predominance of older women, increased body weight, reduced physical activity, weakness of the flexor and extensor muscles of the knee joint and the abductor muscles of the thigh, traumatic cause of amputations at a young age, which does not rule out damage to the of the knee joint, and chronic pain in the knee area.

3. The identification and management of potentially modifiable classical risk factors for the development of OA in the knee joint is one of the rehabilitation tasks for people with disability associated with unilateral transtibial amputation to preserve the functions of the knee joint in the long term and improve the quality of life of this cohort.

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