Osteoarthritis: etiology, epidemiology, impact on the individual and society and the main principles of management

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Key words: osteoarthritis; etiology; epidemiology; impact; principles of management.

Summary. Etiology, epidemiology, and impact of osteoarthritis on an individual, society, and nation and the main principles of management of this disease are reviewed in the article. Treatment should be tailored to the needs of an individual patient. Physicians should be familiar with pharmacologic and nonpharmacologic treatment modalities to maximize effective utilization and a thorough understanding of short- and long-term complications and costs. Severity of osteoarthritis should be taken into physician’s and patient’s consideration while applying an appropriate treatment. A stepwise management of osteoarthritis has to be taken into account. As effective interventions remain underused, state arthritis programs, including osteoarthritis programs, have to be developed to build an appropriate scientific base in public health, observe burden and impact, assess and disseminate evidence-based interventions, and work to reduce and delay disability, and improve quality of life among people with arthritis. Adequate studies on the costs of osteoarthritis are urgently required so that cogent arguments can be made to governments to appropriately fund prevention and treatment programs for this condition. Its recognition as a major cause of disability, particularly in the aging population, should increase community focus on this important condition. Osteoarthritis as a pathogenic process and its impact on an individual and society should be taken into special consideration by health providers and officers developing the national health policy in Lithuania, because there is a lack of information related to the prevalence of osteoarthritis, risk factors, also osteoarthritis-associated disability, and costs of the management of this disease among Lithuanian inhabitants.

Introduction
Osteoarthritis (OA) is the most prevalent form of arthritis presenting as a major source of disability in developed countries. With aging populations, OA is expected to become a serious public health problem. Pain associated with this condition is a chief complaint of most patients, prompting them to seek medical attention (1). Although OA is traditionally thought of as a noninflammatory type of arthritis, with mechanical factors having a central role, inflammatory mechanisms can be present. Pain relief is a main motivator for patients with OA to seek medical attention; however, a secondary benefit of successful treatment is slowing the decrease in patient’s quality of life. Although there is no cure, current strategies are primarily aimed at reducing pain and improving joint function (2, 3). Therefore, the management of OA pain involves both nonpharmacologic and pharmacologic modalities of therapy. Certainly, if these first two modalities are ineffective, the patient should be referred for a surgical evaluation. Preventive strategies to minimize the risk of both the development and progression of OA are therefore of paramount importance not only regarding the issues of quality of life, but the burdening costs of managing and treating this common disorder in the next few decades (4). It is known that the diagnosis of OA is largely clinical, because radiographic findings do not always correlate with symptoms, and consequently knowledge of the etiology and pathogenesis of the disease process aids prevention and management of OA (5).

Definition
OA, also called a degenerative joint disease, is the clinical and pathological outcome of a range of disorders that results in structural and functional failure of synovial joints. It is primarily a disease of the cartilage that ultimately leads to a local tissue response, usually consisting of inflammation, and consequently to mechanical changes that culminate in the failure of these structures to function normally; therefore, the entire joint organ, including the subchondral bone, menisci, ligaments, periarthicular muscle, capsule, and synovium is involved in pathological process (2, 6). Radiographically, OA is characterized by joint space narrowing, osteophytosis, subchondral sclerosis, cyst formation, and abnormal bone contours (7).
Development

OA can develop in any synovial joint in the body, but some sites are more common than others. Interjoint and intrajoint localizations are consistent with the concept that OA is mechanically driven. Within joints, joint damage localizes to the areas that are maximally loaded, and the joints that are most often affected (including the hip, knee, and a thumb base) are those that are not well adapted to upright posture and prehensile grip and therefore suffer mechanically. Thus, OA is mechanically driven. However, this disease process is chemically mediated. The key features of the process, which involve all of the tissues within the synovial joint, include breakdown of the articular cartilage matrix and hypertrophy of marginal and subchondral bone (8).

Etiology and risk factors

It is well known that the etiology of OA is multifactorial, with inflammatory, metabolic, and mechanical causes. A number of environmental risk factors, such as obesity, occupation, low level of education, and trauma, may initiate various pathological pathways (9–12). It has been reported that the correlation between structural changes of the disease and joint symptoms is poor. The risk factors for OA symptoms include bone marrow edema, synovitis, and joint effusion. The role of other less investigated systemic risk factors including bone and bone density; nutrients, particularly those that function as antioxidants; and genetic factors in OA etiology is an object of recent studies (13, 14). In addition, intrinsic factors such as alignment, strength, laxity, and proprioception are currently given more attention (15). Michael et al. have suggested a classification of OA risk factors indicating the role of ethnicity, sports participation, and muscle weakness. Severe joint injury may be sufficient to cause OA; however, the disease is often a consequence of the interplay between systemic and local factors. For example, a person may have an inherited predisposition to develop the disease but will develop it only if a biomechanical insult (such as a knee injury) occurs (Table 1) (16).

Some studies reported that risk factors for OA of different localization may vary. The data of the Osteoarthritis Southern Italy Study (OASIS) involving 1782 patients in Italy demonstrated that hip OA had an important correlation with weight, genetic factors, sex, previous traumas, occupational factors, and age. Knee OA had a great correlation with weight, lifestyle (sedentary lifestyle, cultural or religious aspects of life), and physical activity (17). Similar results were obtained assessing the data of a case-control study among 101 women in Japan, and later these results were compared to the findings of study in carried out in Britain. Heavy weight in the past, constitutional factors, previous injury to the knee, and occupational factors were associated with knee OA in both Britain and Japan, although characteristic activities for work varied (18).

Prevalence

OA is highly prevalent in developed countries. The prevalence of OA increases with age, and sex-specific differences are evident. It has been reported that the incidence and prevalence of disease increase 2 to 10 times from 30 to 65 years of age and keeps increasing thereafter. Up to the age of 50 years, the prevalence of OA in most joints is higher among men than women; however, after the age of 50 years, women more often than men are affected with hand, foot, and knee OA (16). The estimated prevalence of knee pain related to OA in the Spanish general adult population (n=10 291) aged more than 20 years was 10.2% (95% confidence interval [CI], 7.9–12.5), mainly related to a high rate of knee pain in women aged more than 55 years (19). The findings of a large (n=10 291) urban Community Oriented Program for Control of Rheumatic Diseases (COPCORD) study in Iran reported a 41.9% prevalence of rheumatic complaints in the population aged more than 15 years. Degenerative joint diseases were detected in 16.6% of the subjects: cervical spondylosis in 1.8%, knee OA in 15.3%, hand OA in 2.9%, and hip OA in 0.3% (20). The overall prevalence of OA among 3266 Norwegian inhabitants was 12.8% (95% CI, 1.7–14.0), being significantly higher among women than men (14.7% [95% CI, 13.1–16.4] vs. 10.5% [95% CI, 9.0–12.1]). The prevalence of hip OA was 5.5% (95% CI, 4.7–6.3), knee OA 7.1% (95% CI, 6.3–8.0), and hand OA 4.3% (95% CI, 3.6–5.0) (12). The National Arthritis Data Workgroup in the United States reviewed pub-

Table 1. Putative risk factors for osteoarthritis

<table>
<thead>
<tr>
<th>Systematic risk factors</th>
<th>Local biomechanical risk factors</th>
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<tbody>
<tr>
<td>Age</td>
<td>Obesity</td>
</tr>
<tr>
<td>Sex</td>
<td>Joint injury</td>
</tr>
<tr>
<td>Ethnic characteristics lead to susceptibility to osteoarthritis</td>
<td>Joint deformity</td>
</tr>
<tr>
<td>Bone density</td>
<td>Sports participation leads to susceptibility to osteoarthritis</td>
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<tr>
<td>Estrogen replacement therapy in postmenopausal women</td>
<td>Muscle weakness determines the site and severity of osteoarthritis</td>
</tr>
<tr>
<td>Nutritional factors</td>
<td></td>
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<tr>
<td>Genetics</td>
<td>Other systemic factors lead to susceptibility to osteoarthritis</td>
</tr>
</tbody>
</table>
lished analyses from the available national surveys, such as the National Health and Nutrition Examination Survey (NHANES) and the National Health Interview Survey. Nearly 27 million US adults were found to have clinical OA (up from the estimate of 21 million for 1995) (21). Data on all visits of 4 million people to health professionals and hospital admissions covered by the Medical Services Plan (MSP) in British Columbia, Canada, showed that the overall prevalence of OA in 2001 was 10.8%: 8.9% in men and 12.6% in women. The prevalence was higher in women of all age groups. By the age of 70–74 years, about one-third of men and 40% of women had OA (22). A cross-sectional population–based study of 8740 people was conducted in Greece. The age- and sex–adjusted prevalence of symptomatic knee, hand, and hip OA was 6.0% (95% CI, 5.6–6.4), 2% (95% CI, 1.8–2.2), and 0.9% (95% CI, 0.7–1.1), respectively. Symptomatic knee, hand, and hip OA prevalence was significantly higher among women than men and increased significantly with age. Symptomatic knee OA was significantly more common in the rural compared to urban and suburban populations (11). A community–based survey on the prevalence of knee OA and associated factors, involving 2093 residents aged 40 years or more, was carried out in Shanghai, People’s Republic of China. Radiographic knee OA was found in 72.1% of symptomatic and 41.6% of asymptomatic subjects, respectively. The estimated prevalences of symptomatic and asymptomatic knee OA in the community were 7.2% and 37.4%, respectively. Women had a higher symptomatic OA prevalence than men (9.8% vs. 3.7%, P<0.01). The prevalence of symptomatic OA increased with age, from 1.3% in the 40–49–year–old group to 13.2% in the group aged 70 years and more (23). An exploratory study with a cross-sectional design performed in Poland with a randomly selected study population, including 404 (62.9%) rural women and 238 (37.1%) rural men (total 642), showed that 24.6% of the examined population suffered from joint degenerative disease, and OA was diagnosed in 14.7% of participants. The occurrence of OA and joint degenerative disease increased with age and was highest in the group aged more than 50 years (21% and 38.7%, respectively). OA was more frequent in women compared to men (16% and 12.2%, respectively) (24). Unfortunately, there is a lack of published evidence–based data on the prevalence of OA and its main risk factors among Lithuanian inhabitants.

**Diagnosis**

The diagnosis of OA is largely made by obtaining a detailed history and conducting a complete physical examination. Secondary causes, such as calcium deposition; congenital or developmental, endocrine, genetic defects; infectious, metabolic, neuropathic, posttraumatic, and rheumatologic diseases (other than primary osteoarthritis), should be considered when making decisions about having ancillary tests performed. Further evaluation is indicated when the diagnosis remains uncertain, response to therapy is not as expected, or significant clinical changes occur. Clinically indicated laboratory work may include tests for erythrocyte sedimentation and rheumatoid factor (5). Synovial fluid analysis also may be conducted for differential diagnosis to exclude other diagnoses (25). In OA, white blood cell count is usually less than 500 cells/mm$^2$ (0.5 × 10$^9$/L) and is composed predominantly of mononuclear cells. In inflammatory aspirates, white blood cell count is usually greater than 2000 cells/mm$^2$ (2.0 × 10$^9$/L), and usually neutrophils are the predominant cell type. Radiographs can provide objective evidence of the disease. Findings consistent with OA include the presence of joint space narrowing, osteophyte formation, pseudocyst in subchondral bone, and increased density of subchondral bone. The absence of radiographic changes at the onset of the disease, however, does not exclude the diagnosis of OA, but such OA is not clinically significant. Many patients with radiographic changes consistent with OA are asymptomatic or do not exhibit any disability (5).

**Clinical manifestation**

Typically OA presents as joint pain described as exacerbated by activity and relieved by rest. In more advanced disease, it is painful at rest and at night. The source of pain is not particularly well understood and is best framed in a biopsychosocial framework. Due to local events in the joint, the loss of cartilage probably does not contribute directly to pain as it is achemal. On the contrary, the subchondral bone, periosteum, synovium, and joint capsule are all richly innervated and could be the source of nociceptive stimuli in OA (2). In addition, patients describe feeling stiff when arising in the morning with the symptoms lasting no longer 20 to 30 minutes. Furthermore, while sitting during the day or walking some distance, these patients may suffer “gel” phenomenon, which is described as a feeling of stiffness that disappears as a patient begins to move. These symptoms also commonly last no longer than 20 to 30 minutes. Although morning stiffness reduces with the use of the joints, mostly patients with OA appear to acquire more symptoms as the day progresses. Thus, pain increases as the joints are required to bear weight or perform activities throughout the day (6). The data of the AMICA study, Italy, revealed that the most painful OA joints were the knee in 12 827 patients (54%), the hip in 5645 patients (24%), and the hand in 5467 patients (23%) – percentages calculated on the 23 939 patients for whom this information was available (26). Eventually, limitation of joint movement
develops, owing to joint-surface incongruity, capsular contracture, muscle spasm, and mechanical block caused by osteophytes or loose bodies in the joint (7). The joints most commonly involved in the pathological process are knees, hips, feet, ankles, the distal and proximal interphalangeal joints, the first carpometacarpal joints, and low spine. It is unusual for the wrists, elbows, or shoulders to be involved in pathogenic process (6).

Impact
OA is the most prevalent form of arthritis, with an associated risk of mobility disability. With an aging population, this health status is rapidly becoming a significant medical and financial burden to the world due to expensiveness to the individual and society (27, 28). The direct medical costs for the treatment of joint diseases in the United States amount annually to 65 billion dollars, which accounts for 1.4% of gross domestic product (GDP) in the Unites States (29). In France, direct treatment costs exceed 1.6 billion euros annually, equivalent to 1.7% of French health insurance resources, whereas the costs for conservative treatment of OA in Hong Kong amount to 11 690–40 180 Hong Kong dollars per person a year (30, 31). The total cost of conservative treatment for hip and knee OA in Podkarpackie Province, Poland, was 3 347 360 Polish Zloty (PLN) in 2004 and 3 765 980 PLN for a period of 10 months in 2005 (32). Sanitary costs of 314 patients suffering from OA were also calculated in Italy. Total sanitary costs were 455 euros/patient/year; 122 euros was spent on diagnostics, 293 euros on therapy, and 40 euros on management of drug-related gastropathy. Hospitalization accounted for 1/3 of resources, calculated for the management of OA (33). According the data of the Lithuanian State Patients’ Fund at the Ministry of Health, 3321 hip and 2128 knee replacements were performed in Lithuanian hospitals in 2007. About 120 joint replacements are done for 100 000 Lithuanian inhabitants per year; the corresponding numbers in Finland and Norway are 259 and 237, respectively (42). OA also has been implicated as a major cause of admission to nursing homes (43). An increased prevalence of at least a moderately severe depression related to perceived pain, few social contacts, physical limitation of upper and lower body, age, and body mass index is observed among patients with OA and disability caused by this reason in Lithuania.

The main health disorders induced by OA are pain, impaired range of motion (ROM), decreased activities of daily living (ADL); people with OA have less time available for leisure activities and are more dependent on the assistance of family and friends. OA of the knee accounts for more dependence in walking, stair climbing, and other lower-extremity tasks than any other disease (4, 34, 36, 37). The data on 697 participants obtained from a cross-sectional survey carried out in Dicomano, Italy, showed that hip OA was strongly associated with disability in patients aged 65 years and more (38). According to the data of a national survey carried out in France, more than 80% of all patients (n=10 412; mean age, 66.2 years) reported limitations in their ADL for basic tasks, leisure activities, or work. OA patients were substantially more limited than controls: the standardized limitation rate ratios (SLRR) were 6.0 (95% CI, 5.9–6.1) for mobility outside the home, 2.1 (95% CI, 2.0–2.1) for house cleaning, 1.6 (95% CI, 1.5–1.8) for dressing oneself, and 1.6 (95% CI, 1.5–1.8) for sports. Of the 17.6% of OA patients and 17.5% of the controls still working, 64.4% and 14.3%, respectively, were limited in their job duties, for a SLRR of 4.5 (95% CI, 4.3–4.7). This study showed that OA-related disability had a significant impact on the retired as well as on those still involved in the labor market (37). Patients with OA more frequently use healthcare providers’ help due to poor health status: fatigue, emotional distress, sick leaves more than 8 weeks, pain duration more than one year, and higher expenditures on healthcare are more frequently documented among patients with OA than age–matched and sex–matched peers in the general population (12).

OA is also indicated as the most common reason for total hip and knee replacement. It is estimated that 85% of all knee replacements are carried out for patients with OA. About 19 000 hip and 20 000 knee replacements are being performed in Australia due to osteoarthritis each year (34, 39–41). According the data of the Lithuanian State Patients’ Fund at the Ministry of Health, 3321 hip and 2128 knee replacements were performed in Lithuanian hospitals in 2007. About 120 joint replacements are done for 100 000 Lithuanian inhabitants per year; the corresponding numbers in Finland and Norway are 259 and 237, respectively (42). OA also has been implicated as a major cause of admission to nursing homes (43). An increased prevalence of at least a moderately severe depression related to perceived pain, few social contacts, physical limitation of upper and lower body, age, and body mass index is observed among patients with OA (44). The data of the Johnston County Osteoarthritis Project (n=2682) indicate that symptomatic hip and knee OA were significantly associated with sleep problems, independent of other factors related to sleep difficulties, including self-rated health and depression; therefore, it is recommended to screen patients with OA regularly for sleep disturbances as a part of routine care (45). Patients with a clinical diagnosis of knee OA and with knee pain have an increased risk of nonvertebral and hip fracture; also, radiographic knee OA is associated with an increased risk of incident vertebral and nonvertebral fractures as...
well. Knee pain and OA should be regarded as independent risk factors for fracture (46, 47).

**Principles of osteoarthritis management**

The combination of aging population, increased obesity, and increasing joint damage causes a rising burden of OA worldwide in this century. The recent review of the World Health Organization on the impact of diseases noted that musculoskeletal disorders take the fourth most common cause of loss of disability-adjusted life years (DALY’s), with OA making the greatest contribution. These facts suggest that urgent measures should be taken to prevent OA.

Prevention could be primary (reduction of risk factors so that fewer people would develop this condition), secondary (introduction of interventions that prevent progression to serious disease), and tertiary (treatment of consequences of the condition) (8, 48). The aims of treatment are as follows:

- To educate patients about the disease and its management;
- To control pain adequately;
- To improve function;
- To alter the disease process and its consequences.

A variety of theoretical targets for these approaches can be considered, including:

- The joints themselves;
- Other parts of the musculoskeletal system (subchondral bone, osteophytes, ligament, enthesis, joint capsule, periarticular muscle, synovium);
- The peripheral or central nervous system;
- Psychosocial factors;
- Comorbidity.

OA should be managed on an individual basis and will probably consist of a combination of treatment options. Treatment should be comprehensive and modified according to the obtained response; therefore, the five issues should be taken in consideration choosing a right modality of treatment:

- Age;
- Comorbidity;
- Clinical severity;
- Individual preferences;
- Costs.

Many different treatments are available to people who have OA and are provided by a number of health professional groups including nurse specialists, physiotherapists, occupational therapists, podiatrists, orthotists, psychologists, general practitioners, dietitians, rheumatologists, orthopedic surgeons, and practitioners of complementary and alternative medicine. A classification of the therapeutic options available for the management of OA is presented in Table 2 (2, 8, 49–51).

**Table 2. Classification of the treatment modalities available for the management of osteoarthritis**

<table>
<thead>
<tr>
<th>Treatment modality</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Educational, lifestyle, and behavioral</td>
<td>Education of a patient, spouse, family, and other important family members</td>
</tr>
<tr>
<td></td>
<td>Empowerment to aid patients in self-management and taking control</td>
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<td></td>
<td>Behavioral and environmental changes to reduce the impact of osteoarthritis</td>
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<td></td>
<td>Social support including telephone contact</td>
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<td></td>
<td>Alteration of levels of general exercise and activities</td>
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<td></td>
<td>Weight loss</td>
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<tr>
<td></td>
<td>Use of different shoes, orthoses, canes, other walking aids and assistive devices</td>
</tr>
<tr>
<td>Other nonpharmacologic measures</td>
<td>Physical aids to help joint protection and improve function</td>
</tr>
<tr>
<td></td>
<td>Podiatry</td>
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<tr>
<td></td>
<td>Acupuncture</td>
</tr>
<tr>
<td></td>
<td>Transcutaneous nerve stimulation and acupuncture</td>
</tr>
<tr>
<td></td>
<td>Dietary supplements including glucosamine, chondroitin, vitamins C and D, ginger extracts, avocado, soybean derivatives. Nevertheless, the effectiveness of dietary supplements has not been proved yet</td>
</tr>
<tr>
<td>Pharmacologic measures</td>
<td>Nonopioid type analgesics (e.g., paracetamol, nonsteroidal anti-inflammatory drugs [NSAIDs] including coxibs)</td>
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<tr>
<td></td>
<td>Antidepressants for analgesia and depression</td>
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<tr>
<td></td>
<td>Opioid-type analgesics (morphine, hydromorphone, oxymorphone*, tramadol, codeine, and many others)</td>
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<tr>
<td></td>
<td>Topical agents including capsaicin and NSAID creams and gels (also as accompanying treatment)</td>
</tr>
<tr>
<td></td>
<td>Intra-articular injections including steroids and hyaluronic acid</td>
</tr>
<tr>
<td></td>
<td>Diacerhein**</td>
</tr>
<tr>
<td>Surgical measures</td>
<td>Tidal irrigation (washout) of the joint (in knee osteoarthritis)</td>
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<tr>
<td></td>
<td>Arthroscopic debridement</td>
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<tr>
<td></td>
<td>Cartilage transplantation and tissue engineering techniques</td>
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<tr>
<td></td>
<td>Osteotomy</td>
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<td></td>
<td>Partial or complete joint replacement</td>
</tr>
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</table>

*Oxymorphone (elsewhere – Opana®, Opana ER®) extended-release tablets are indicated for the management of chronic pain of all or most etiologies and are indicated only for patients already administered a regular regimen of strong opioids for a prolonged period. **Diacerhein and rhein are anthraquinone compounds that ameliorate the course of osteoarthritis. Recent reports also suggest that these compounds may have anti-inflammatory properties, but the cellular mechanisms by which they exert antiosteoarthritic and possibly anti-inflammatory effects are still incompletely understood.
Despite the effectiveness of pharmacologic approaches to the management of pain in OA, the undesirable side effects are documented; therefore, choosing an appropriate nonsteroidal anti-inflammatory agent it is essential to consider the risk of gastrointestinal as well cardiovascular damage (52).

It is important to remember that the recommended hierarchy of disease management should start from nonpharmacologic treatment first. The first step is forgotten frequently or not emphasized sufficiently to the patient’s detriment. A stepwise management of patients with OA considering the severity of disease is offered in Table 3 (2, 8).

Table 3. A stepwise management of patients with osteoarthritis

<table>
<thead>
<tr>
<th>Category of osteoarthritis (severity of symptoms)</th>
<th>Suggested stepwise management strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Nonpharmacologic: education, exercise, weight loss, appropriate footwear</td>
</tr>
<tr>
<td>Moderate with no other problems</td>
<td>Nonpharmacologic: physiotherapy, braces, education, advice, consideration of appropriate changes in lifestyle and diet, and pharmacologic treatment with nonopioid analgesics (such as paracetamol)</td>
</tr>
<tr>
<td>Mild or moderate complicated by other health problems</td>
<td>Pharmacologic management: nonopioid analgesics (NSAIDs), opioid analgesics (if effusion is present, aspirate and inject); treatment of comorbidities is often much more effective than treating osteoarthritis</td>
</tr>
<tr>
<td>Severe</td>
<td>Surgery: osteotomy, total joint replacement</td>
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</tbody>
</table>

Concluding remarks

1) Treatment should be tailored to the needs of the individual patient. Physicians should be familiar with pharmacologic and nonpharmacologic treatment modalities to maximize effective utilization and a thorough understanding of the short- and long-term complications and costs.

2) Severity of osteoarthritis should be taken into physician’s and patient’s consideration applying an appropriate treatment. A stepwise management of osteoarthritis has to be taken into account.

3) As effective interventions remain underused, state arthritis programs, including osteoarthritis programs, have to be developed to build an appropriate scientific base in public health, observe burden and impact, assess and disseminate evidence-based interventions, and work to reduce and delay disability, and improve quality of life among people with arthritis.

4) Adequate studies on the costs of osteoarthritis are urgently required so that cogent arguments can be made to governments to appropriately fund prevention and treatment programs for this condition. Its recognition as a major cause of disability, particularly in the aging population, should increase community focus on this important condition.

5) Osteoarthritis as a pathogenic process and its impact on an individual and society should be taken into special consideration by health providers and officers developing the national health policy in Lithuania, because there is a lack of information related to the prevalence of osteoarthritis, risk factors, also osteoarthritis-associated disability, and costs of the management of this disease among Lithuanian inhabitants.

Osteoarthritis: etiology, epidemiology, impact on the individual and society and management

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Raktažodžiai: osteoarthritis, etiologija, epidemiologija, įtaka, gydymo principai.


Medicina (Kaunas) 2010; 46(11)
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Received 30 September 2009, accepted 8 November 2010
 Straipsnis gautas 2009 09 30, priimtas 2010 11 08

Medicina (Kaunas) 2010; 46(11)