Osteoarthritis

Osteoarthritis (**OA**) also known as **degenerative arthritis**, **degenerative joint disease**, or **osteoarthrosis**, is a type of joint disease that results from breakdown of joint cartilage and underlying bone.[1] The most common symptoms are joint pain and stiffness. Initially, symptoms may occur only following exercise, but over time may become constant. Other symptoms may include joint swelling, decreased range of motion, and when the back is affected weakness or numbness of the arms and legs. The most commonly involved joints are those near the ends of the fingers, at the base of the thumb, neck, lower back, knees, and hips. Joints on one side of the body are often more affected than those on the other. Usually the problems come on over years. It can affect work and normal daily activities. Unlike other types of arthritis, only the joints are typically affected.[2]

Causes include previous joint injury, abnormal joint or limb development, and inherited factors. Risk is greater in those who are overweight, have one leg of a different length, and have jobs that result in high levels of joint stress.[2][3] Osteoarthritis is believed to be caused by mechanical stress on the joint and low grade inflammatory processes.[4] It develops as cartilage is lost with eventually the underlying bone becoming affected.[2] As pain may make it difficult to exercise, muscle loss may occur.[3][5] Diagnosis is typically based on signs and symptoms with medical imaging and other tests occasionally used to either support or rule out other problems. Unlike in rheumatoid arthritis, which is primarily an inflammatory condition, the joints do not typically become hot or red.[2]

Treatment includes exercise, efforts to decrease joint stress, support groups, and pain medications. Efforts to decrease joint stress include resting, the use of a cane, and braces. Weight loss may help in those who are overweight. Pain medications may include paracetamol (acetaminophen). If this does not work NSAIDs such as naproxen may be used but these medications are associated with greater side effects. Opioids if used are generally only recommended short term due to the risk of addiction.[2] If pain interferes with normal life despite other treatments, joint replacement surgery may help. An artificial joint, however, only lasts a limited amount of time.[3] Outcomes for most people with osteoarthritis are good.[2]

OA is the most common form of arthritis with disease of the knee and hip affecting about 3.8% of people as of 2010.[2][6] Among those over 60 years old about 10% of males and 18% of females are affected.[3] It is the cause of about 2% of years lived with disability.[6] In Australia about 1.9 million people are affected,[7] and in the United States about 27 million people are affected.[2] Before 45 years of age it is more common in men, while after 45 years of age it is more common in women. It becomes more common in both sexes as people become older.[2]

1 Signs and symptoms

The main symptom is pain, causing loss of ability and often stiffness. "Pain" is generally described as a sharp ache or a burning sensation in the associated muscles and tendons. OA can cause a crackling noise (called "crepitus") when the affected joint is moved or touched and people may experience muscle spasms and contractions in the tendons. Occasionally, the joints may also be filled with fluid.[8] Some people report increased pain associated with cold temperature, high humidity, and/or a drop in barometric pressure, but studies have had mixed results.[9]

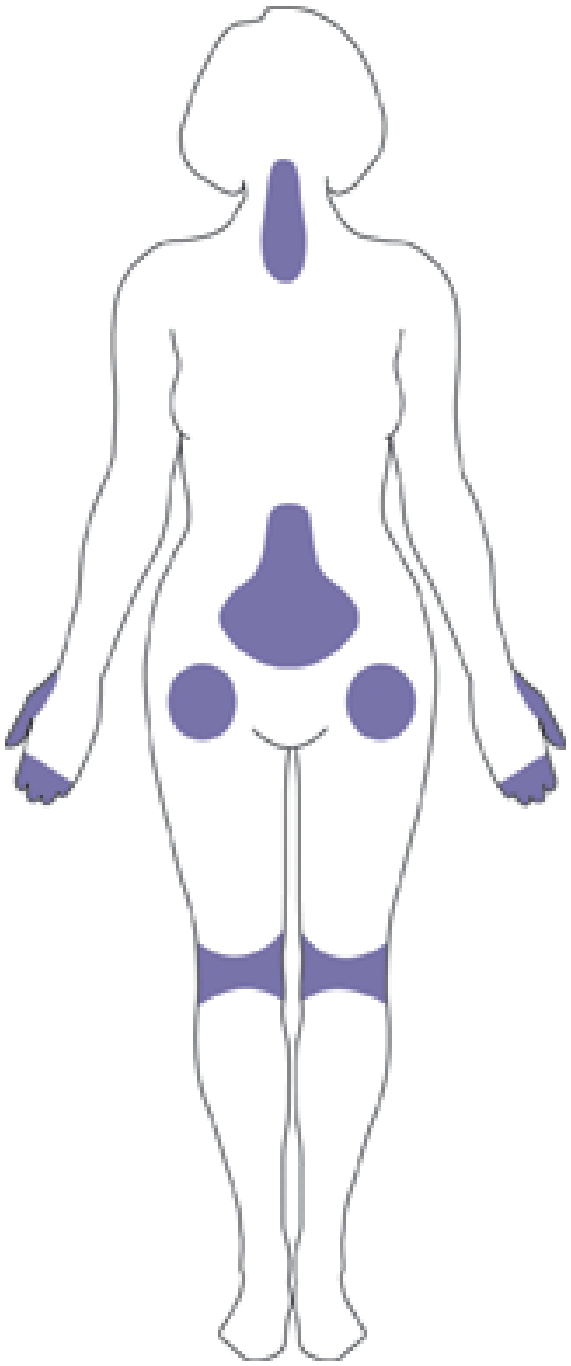
OA commonly affects the hands, feet, spine, and the large weight bearing joints, such as the hips and knees, although in theory, any joint in the body can be affected. As OA progresses, the affected joints appear larger, are stiff and painful, and usually feel better with gentle use but worse with excessive or prolonged use, thus distinguishing it from rheumatoid arthritis.

In smaller joints, such as at the fingers, hard bony enlargements, called Heberden's nodes (on the distal interphalangeal joints) and/or Bouchard's nodes (on the proximal interphalangeal joints), may form, and though they are not necessarily painful, they do limit the movement of the fingers significantly. OA at the toes leads to the formation of bunions, rendering them red or swollen. Some people notice these physical changes before they experience any pain.

OA is the most common cause of a joint effusion of the knee.[10]

2 Risk factors

Damage from mechanical stress with insufficient self repair by joints is believed to be the primary cause of osteoarthritis.[11] Sources of this stress may include misalignments of bones caused by congenital or pathogenic causes; mechanical injury; excess body weight; loss of strength in the muscles supporting a joint; and impair-



Osteoarthritis most often occurs in the hands (at the ends of the fingers and thumbs), neck, lower back, knees, and hips

ment of peripheral nerves, leading to sudden or uncoordinated movements.[11] However exercise, including running in the absence of injury, has not been found to increase the risk.[12] Nor has cracking one's knuckles been found to play a role.[13]

2.1 Primary

A number of studies have shown that there is a greater prevalence of the disease among siblings and especially identical twins, indicating a hereditary basis.[14] Although a single factor is not generally sufficient to cause the disease, about half of the variation in susceptibility has been assigned to genetic factors.[15]

As early human ancestors evolved into bipeds, changes occurred in the pelvis, hip joint and spine which increased the risk of osteoarthritis.[16] Additionally genetic variations that increase the risk were likely not selected against because usually problems only occur after reproductive success.[17]

The development of OA is correlated with a history of previous joint injury and with obesity, especially with respect to knees.[18] Since the correlation with obesity has been observed not only for knees but also for non-weight bearing joints and the loss of body fat is more closely related to symptom relief than the loss of body weight, it has been suggested that there may be a metabolic link to body fat as opposed to just mechanical loading.[19]

Changes in sex hormone levels may play a role in the development of OA as it is more prevalent among post-menopausal women than among men of the same age.[20][21] A study of mice found natural female hormones to be protective while injections of the male hormone dihydrotestosterone reduced protection.[22]

2.2 Secondary

lateral

front

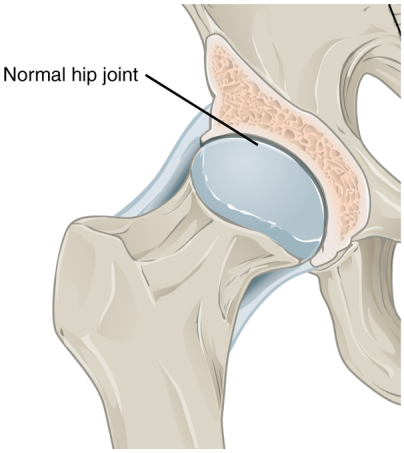
Secondary osteoarthritis (due to an old injury with fracture) of the ankle in a woman of 82 years old

This type of osteoarthritis is caused by other factors but the resulting pathology is the same as for primary os-

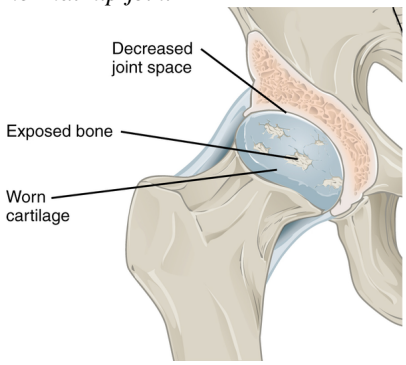
teoarthritis:

- Alkaptonuria
- Congenital disorders of joints
- Diabetes doubles the risk of having a joint replacement due to OA and people with diabetes have joint replacements at a younger age than those without diabetes.[23]
- Ehlers-Danlos Syndrome
- Hemochromatosis and Wilson's disease
- Inflammatory diseases (such as Perthes' disease), (Lyme disease), and all chronic forms of arthritis (e.g., costochondritis, gout, and rheumatoid arthritis). In gout, uric acid crystals cause the cartilage to degenerate at a faster pace.
- Injury to joints or ligaments (such as the ACL), as a result of an accident or orthopedic operations.
- Ligamentous deterioration or instability may be a factor.
- Marfan syndrome
- Obesity
- Joint infection

3 Pathophysiology



Normal hip joint



Hip joint with osteoarthritis[24]

While OA is a degenerative joint disease that may cause gross cartilage loss and morphological damage to other joint tissues, more subtle biochemical changes occur in the earliest stages of OA progression. The water content of healthy cartilage is finely balanced by compressive force driving water out & swelling pressure drawing water in.[25] Collagen fibres exert the compressive force, whereas the Gibbs–Donnan effect & cartilage proteoglycans create osmotic pressure which tends to draw water in.[25]

However, during onset of OA, the collagen matrix becomes more disorganized and there is a decrease in proteoglycan content within cartilage. The breakdown of collagen fibers results in a net increase in water content.[26][27][28][29][30] This increase occurs because whilst there is an overall loss of proteoglycans (and thus a decreased osmotic pull),[27][31] it is outweighed by a loss of collagen.[25][31] Without the protective effects of the proteoglycans, the collagen fibers of the cartilage can become susceptible to degradation and thus exacerbate the degeneration. Inflammation of the synovium (joint cavity lining) and the surrounding joint capsule can also occur, though often mild (compared to what occurs in rheumatoid arthritis). This can happen as breakdown products from the cartilage are released into the synovial space, and the cells lining the joint attempt to remove them.

Other structures within the joint can also be affected.[32] The ligaments within the joint become thickened and fibrotic and the menisci can become damaged and wear away.[33] Menisci can be completely absent by the time a person undergoes a joint replacement. New bone outgrowths, called "spurs" or osteophytes, can form on the margins of the joints, possibly in an attempt to improve the congruence of the articular cartilage surfaces in the absence of the menisci. The subchondral bone volume increases and becomes less mineralized (hypomineralization).[34] All these changes can cause problems functioning. The pain in an osteoarthritic joint has been related to thickened synovium[35] and subchondral bone lesions.[36]

4 Diagnosis

Diagnosis is made with reasonable certainty based on history and clinical examination.[37][38] X-rays may confirm the diagnosis. The typical changes seen on X-ray include: joint space narrowing, subchondral sclerosis (increased bone formation around the joint), subchondral cyst formation, and osteophytes.[39] Plain films may not correlate with the findings on physical examination or with the degree of pain.[40] Usually other imaging techniques are not necessary to clinically diagnose OA.

In 1990, the American College of Rheumatology, using

data from a multi-center study, developed a set of criteria for the diagnosis of hand OA based on hard tissue enlargement and swelling of certain joints.[41] These criteria were found to be 92% sensitive and 98% specific for hand OA versus other entities such as rheumatoid arthritis and spondyloarthropathies.[42]

Related pathologies whose names may be confused with OA include pseudo-arthrosis. This is derived from the Greek words pseudo, meaning "false", and arthrosis, meaning "joint." Radiographic diagnosis results in diagnosis of a fracture within a joint, which is not to be confused with OA which is a degenerative pathology affecting a high incidence of distal phalangeal joints of female patients. A polished ivory-like appearance may also develop on the bones of the affected joints, reflecting a change called eburnation.[43]

- Severe osteoarthritis and osteopenia of the carpal joint and 1st carpometacarpel joint.
- MRI of osteoarthritis in the knee, with characteristic narrowing of the joint space.
- Primary osteoarthritis of the left knee. Note the osteophytes, narrowing of the joint space (arrow), and increased subchondral bone density (arrow).
- Damaged cartilage from sows. (a) cartilage erosion (b)cartilage ulceration (c)cartilage repair (d)osteophyte (bone spur) formation.
- Histopathology of osteoarthrosis of a knee joint in an elderly female.
- Histopathology of osteoarthrosis of a knee joint in an elderly female.
- In a healthy joint, the ends of bones are encased in smooth cartilage. Together, they are protected by a joint capsule lined with a synovial membrane that produces synovial fluid. The capsule and fluid protect the cartilage, muscles, and connective tissues.
- With osteoarthritis, the cartilage becomes worn away. Spurs grow out from the edge of the bone, and synovial fluid increases. Altogether, the joint feels stiff and sore.
- thumb|Osteoarthritis

4.1 Classification

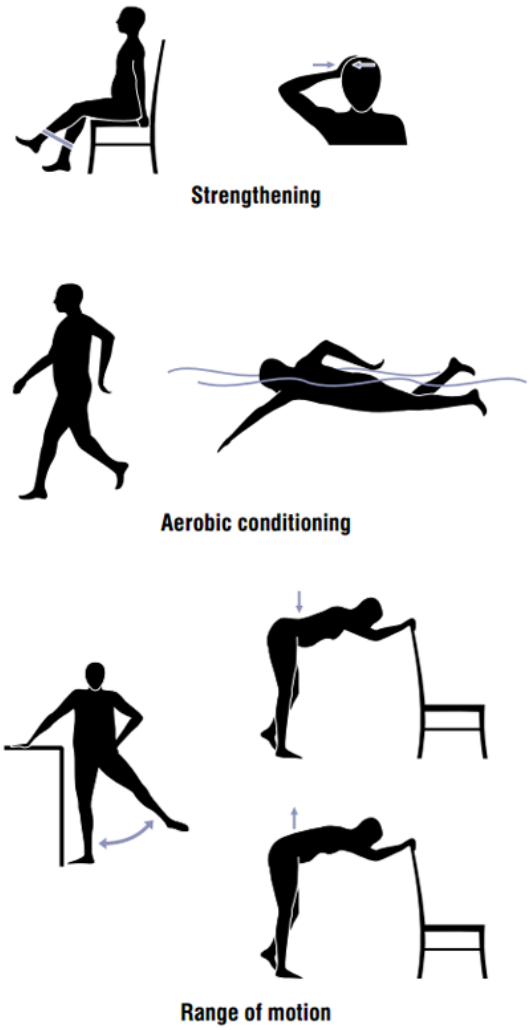
A number of classification systems are used for gradation of osteoarthritis:

- WOMAC scale
- Kellgren-Lawrence grading scale

OA can be classified into either primary or secondary depending on whether or not there is an identifiable underlying cause.

Both primary generalized nodal OA and erosive OA (EOA, also called inflammatory OA) are sub-sets of primary OA. EOA is a much less common, and more aggressive inflammatory form of OA which often affects the distal interphalangeal joints of the hand and has characteristic articular erosive changes on x-ray.[44]

5 Management



People with osteoarthritis should do different kinds of exercise for different benefits to the body.

Lifestyle modification (such as weight loss and exercise) and analgesics are the mainstay of treatment. Acetaminophen (also known as paracetamol) is recommended first line with NSAIDs being used as add on therapy only if pain relief is not sufficient.[45] This is due to the relative greater safety of acetaminophen.[45]

5.1 Lifestyle modification

For overweight people, weight loss may be an important factor.[46] Patient education has been shown to be helpful in the self-management of arthritis.[46] It decreases pain, improves function, reduces stiffness and fatigue, and reduces medical usage.[46] Patient education can provide on average 20% more pain relief when compared to NSAIDs alone in patients with hip OA.[46]

5.2 Physical measures

Moderate exercise is beneficial with respect to pain and function in those with osteoarthritis of the knee and hip.[47][48] These exercises should occur at least three times per week.[49] While some evidence supports certain physical therapies, evidence for a combined program is limited.[50] There is not enough evidence to determine the effectiveness of massage therapy.[51] The evidence for manual therapy is inconclusive.[52] Functional, gait, and balance training has been recommended to address impairments of position sense, balance, and strength in individuals with lower extremity arthritis as these can contribute to higher falls in older individuals.[53]

Lateral wedge insoles do not appear to be useful in osteoarthritis of the knee.[54][55] Knee braces may be useful.[56] For pain management heat can be used to relieve stiffness, and cold can relieve muscle spasms and pain.[57]

5.3 Medication

The analgesic acetaminophen is the first line treatment for OA.[45][59] However, a 2015 review found acetaminophen to only have a small short term benefit.[60] For mild to moderate symptoms effectiveness is similar to non-steroidal anti-inflammatory drugs (NSAIDs), though for more severe symptoms NSAIDs may be more effective.[45] NSAIDs such as naproxen while more effective in severe cases are associated with greater side effects such as gastrointestinal bleeding.[45] Another class of NSAIDs, COX-2 selective inhibitors (such as celecoxib) are equally effective to NSAIDs with lower rates of adverse gastrointestinal effects but higher rates of cardiovascular disease such as myocardial infarction.[61] They are also more expensive than non-specific NSAIDs.[62] Oral opioids, including both weak opioids such as tramadol and stronger opioids, are also often prescribed. Their appropriateness is uncertain and opioids are often recommended only when first line therapies have failed or are contraindicated.[63][63][64] This is due to a small benefit and relatively large risk of side effects.[65] Oral steroids are not recommended in the treatment of OA.[59]

There are several NSAIDs available for topical use including diclofenac. Topical and oral diclofenac work equally well with topical having a greater risk of mild skin reactions but no greater risk of gastrointestinal adverse effects.[66] Transdermal opioid pain medications are not typically recommended in the treatment of osteoarthritis.[67] Topical capsaicin is controversial with some reviews finding benefit[68][69] and others not.[70]

Joint injections of glucocorticoids (such as hydrocortisone) leads to short term pain relief that may last between a few weeks and a few months.[71] Injections of hyaluronic acid have not been found to lead to much improvement compared to placebo[72][73] but have been associated with harm.[73] The effectiveness of injections of platelet-rich plasma is unclear; there are suggestions that such injections improve function but not pain and are associated with increased risk.[74][75]

5.4 Surgery

If problems are significant and more conservative management is ineffective, joint replacement surgery or resurfacing may be recommended. Evidence supports joint replacement for both knees and hips as it is both clinically effective,[76][77] and cost-effective.[78][79] Surgery to transfer articular cartilage from a non-weight-bearing area to the damaged area is one possible procedure that has some success but there are problems getting the transferred cartilage to integrate well with the existing cartilage at the transfer site.[80]

Osteotomy may be useful in people with knee osteoarthritis but has not been well studied.[81] Arthroscopic surgery is largely not recommended as it does not improve outcomes in knee osteoarthritis.[82][83] Additionally arthroscopy may result in harm.[84]

5.5 Alternative medicine

Many dietary supplements are sold as treatments for OA. Since glucosamine is a precursor for a component of cartilage, it has been studied for prevention and treatment. The effectiveness of glucosamine is controversial.[85][86] Most recent reviews found it to be equal to[87][88] or only slight better than placebo.[89][90] A difference may exist between glucosamine sulfate and glucosamine hydrochloride, with glucosamine sulfate showing a benefit and glucosamine hydrochloride not.[91] The evidence for glucosamine sulfate having an effect on OA progression is somewhat unclear and if present likely modest.[92] The Osteoarthritis Research Society International recommends that glucosamine be discontinued if no effect is observed after six months[93] and the National Institute of Clinical Excellence no longer recommends its use.[5] Despite the difficulty in determining the efficacy of glucosamine, it remains a viable treatment option.[94] Its use as a therapy for osteoarthritis is usually safe.[94]

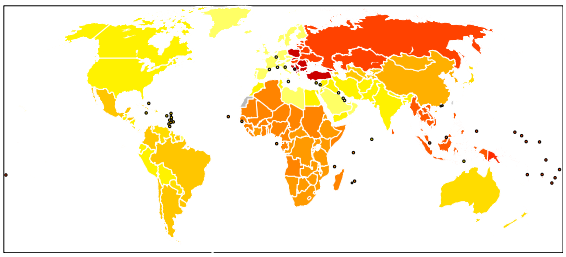
Phytodolor,[68] SAMe,[95] and SKI 306X (a Chinese herbal mixture)[69] may be effective in improving pain, and there is some evidence to support the use of cat's claw as an anti-inflammatory.[96] There is tentative evidence to support avocado/soybean unsaponifiables (ASU),[69][97] methylsulfonylmethane,[68] and rose hip.[68] A few high-quality studies of *Boswellia serrata* show consistent, but small, improvements in pain and function among people with osteoarthritis.[98]

There is little evidence supporting benefits for some supplements, including: the Ayurvedic herbal preparations with brand names Articulin F and Eazmov, collagen, devil's claw, Duhuo Jisheng Wan (a Chinese herbal preparation), fish liver oil, ginger, the herbal preparation gitadyl, glucosamine, hyaluronic acid, omega-3 fatty acids, the brand-name product Reumalax, stinging nettle, turmeric, vitamins A, C, and E in combination, vitamin E alone, vitamin K and willow bark. There is insufficient evidence to make a recommendation about the safety and efficacy of these treatments.[68][96]

While acupuncture leads to improvements in pain relief, this improvement is small and may be of questionable importance. Waiting list-controlled trials for peripheral joint osteoarthritis do show clinically relevant benefits, but these may be due to placebo effects.[99] Acupuncture does not seem to produce long-term benefits.[100] While electrostimulation techniques such as TENS have been used for twenty years to treat osteoarthritis in the knee, there is no conclusive evidence to show that it reduces pain or disability.[101]

A Cochrane review of low level laser therapy found unclear evidence of benefit.[102] Another review found short term pain relief for osteoarthritic knees.[103]

6 Epidemiology



Disability-adjusted life year for OA per 100,000 inhabitants in 2004.[104]

Globally approximately 250 million people have osteoarthritis of the knee (3.6% of the population).[105] OA affects nearly 27 million people in the United States, accounting for 25% of visits to primary care physicians, and half of all NSAID prescriptions. It is estimated that 80% of the population have radiographic evidence of OA by age 65, although only 60% of those will have symptoms.[106]

As of 2004, OA globally causes moderate to severe disability in 43.4 million people.[107]

In the United States, there were approximately 964,000 hospitalizations for osteoarthritis in 2011, a rate of 31 stays per 10,000 population.[108] With an aggregate cost of $14.8 billion ($15,400 per stay), it was the second-most expensive condition seen in U.S. hospital stays in 2011. By payer, it was the second-most costly condition billed to Medicare and private insurance.[109][110]

7 History

Evidence for OA found in the fossil record is studied by paleopathologists, specialists in ancient disease and injury. OA has been reported in fossils of the large carnivorous dinosaur *Allosaurus fragilis*.[111]

7.1 Etymology

OA is derived from the Greek word part *osteo-*, meaning "of the bone", combined with *arthritis*: *arthr-*, meaning "joint", and *-itis*, the meaning of which has come to be associated with inflammation.[112] The *-itis* of OA could be considered misleading as inflammation is not a conspicuous feature. Some clinicians refer to this condition as *osteoarthosis* to signify the lack of inflammatory response.

8 Research

There are ongoing efforts to determine if there are agents that modify outcomes in OA. Sprifermin is one candidate drug. There is also tentative evidence that strontium ranelate may decrease degeneration in OA and improve outcomes.[113][114]

As well as attempting to find disease-modifying agents for OA, there is emerging evidence that a system-based approach is necessary to find the causes of OA.[115] Changes may occur before clinical disease is evident due to abnormalities in biomechanics, biology and/or structure of joints that predispose them to develop clinical disease. Research is thus focusing on defining these early pre-OA changes using biological, mechanical, and imaging markers of OA risk, emphasising multi-disciplinary approaches, and looking into personalized interventions that can reverse OA risk in healthy joints before the disease becomes evident.

Gene transfer strategies aim to target the disease process rather than the symptoms.[116]

8.1 Biomarkers

Guidelines outlining requirements for inclusion of soluble biomarkers in OA clinical trials were published in 2015,[117] but as yet, there are no validated biomarkers for OA. A 2015 systematic review of biomarkers for OA looking for molecules that could be used for risk assessments found 37 different biochemical markers of bone and cartilage turnover in 25 publications.[118] The strongest evidence was for urinary C-terminal telopeptide of collagen type II (uCTX-II) as a prognostic marker for knee OA progression and serum cartilage oligomeric protein (COMP) levels as a prognostic marker for incidence of both knee and hip OA. A review of biomarkers in hip OA also found associations with uCTXII.[119]

One problem with using a specific collagen type II biomarker from the breakdown of articular cartilage is that the amount of cartilage is reduced (worn away) over time with progression of the disease so a patient can eventually have very advanced OA with none of this biomarker detectable in their urine. Another problem with a systemic biomarker is that a patient can have OA in multiple joints at different stages of disease at the same time, so the biomarker source cannot be determined. Some other collagen breakdown products in the synovial fluid correlated with each other after acute injuries (a known cause of secondary OA) but did not correlate with the severity of the injury.[120]

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10 External links

- American College of Rheumatology Factsheet on OA
- Osteoarthritis The Arthritis Foundation
- National Institute of Arthritis and Musculoskeletal and Skin Diseases - US National Institute of Arthritis and Musculoskeletal and Skin Diseases

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11.1 Text

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