

Knee osteoarthritis diagnosis, treatment and associated factors of progression: part II

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Abstract

Diagnosis of knee osteoarthritis can be confirmed based on clinical and/or radiological features. The potential of a progressive disease can be prevented or decreased by earlier recognition and correction of associated factors. Obesity and alignment especially varus malalignment are recognized factors of a progressive disease. Both nonpharmacological as well as pharmacological modalities of treatment are useful in managing the symptoms of knee osteoarthritis. Surgery should be considered only in patients who do not respond to medical therapy. The prevalence and risk factors of knee osteoarthritis have been described in the first part of this review. In this issue, the diagnosis progressive factors and management of knee osteoarthritis are discussed.

Key words: Knee osteoarthritis, Progressive factors, Malalignment, Varus deformity, Valgus deformity.

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Early recognition of patients with knee OA and correction of risk factors is important. Diagnosis can be made based on history and clinical features (table 1) (2). However, in a number of patients especially in patients with suspected clinical features, confirmation of OA or determining the extent of joint involvement may require performance of radiography or MRI examinations. Information with regard to some clinical features and risk factors such as age, sex, body mass index, absence of whole leg pain, traumatic onset, difficulties in descending the stairs, palpable effusion, fixed-flexion deformity, restricted-flexion range of motion, and crepitus are helpful and predict the development of radiographic findings in favor of knee OA with a sensitivity and a specificity of 94% and 93%, respectively (56). Diagnosis of knee may also be possible according to the American College of Rheumatology criteria (table 1), as well as by using EULAR diagnostic criteria (57). Based on the latter criteria the presence of 3 symptoms (persistent knee pain, limited morning stiffness and reduce function), and 3 signs (crepitus, restricted movement and bony enlargement) can correctly diagnose 99% of knee OA when all 6 symptoms and signs are present.

Differential diagnosis

Several conditions should be considered in the differential diagnosis of knee OA. Septic arthritis, inflammatory articular diseases can be ruled out by the pattern of joint involvement and appropriate clinical features and laboratory tests. Bilateral symmetrical small joint pain, swelling and stiffness should arouse the suspicion of RA. The wrist and the knee are commonly affected by pseudogout and the first metatarsophalangeal joint or knee joint involvement may be seen in patients with gout. Stiffness in the shoulder and hip girdles exacerbated in the morning is suggestive of polymyalgia rheumatica. When a definitive diagnosis of knee OA has been made, further investigations in regard to laboratory test are not required.

However, in suspected cases tests such as CBC, ESR and CRP, uric acid may provide further diagnostic facilities and performance of x-rays for the affected joints especially following trauma, may be helpful for definitive diagnosis (58). Pes anserinus tendinitis/bursitis is a frequent cause of knee pain in patients with knee OA which should be considered in patients with localized periarticular symptoms or signs. Valgus deformity increases the possibility of this condition by 5.2 times and collateral instability increases the development of tendinitis/bursitis by 6 times (59).

Table 1. American College of Rheumatology criteria for the diagnosis of knee osteoarthritis

Using history and clinical examination*

Pain in the knee and three of the following

- 1-Age >50 years
- 2- Morning stiffness <30 minutes
- 3-Crepitus on active motions
- 4-Bony tenderness
- 5-Bony enlargement
- 6-No palpable warmth of synovium

Using history and clinical examination and radiographic findings

Pain in the knee and one of the following

- 1-Age >50 years
- 2- Morning stiffness < 30 minutes
- 3-Crepitus on active motions and osteophyte

Using history and clinical examination and laboratory findings

Pain in the knee and 5 of the following

- 1- Age >50 years
- 2- Morning stiffness <30 minutes
- 3-Crepitus on active motions
- 4-Bony enlargement
- 5-No palpable warmth of synovium
- 6-ESR <40 mm/h
- 7-Rheumatoid Factor <1/40
- 8-Synovial fluid signs of osteoarthritis

*Reference: Altman, R, et al.: Arthritis Rheum 29:1039, 1986.

The course of knee OA and factors of progression

A proportion of patients with knee OA have a progressive course. The rate of progression varies across the life stages based on the presence or absence of some associated factors. In the elderly persons, the rate of progression is low (60). In Framingham study, over a mean follow up period of 8.1 years, a progressive rate of 4% per year was observed among patients with knee OA. In another study of 32 patients with knee OA who were followed up for 2 years, about 6.1% of cartilage volume had lost over the study period. In this study, progression of knee OA was evident as early as six months after the start of the study (61).

Progression of OA may be attributed to the effects of biomechanical forces derived in response to pathological reactions. These factors can lead to progressive deterioration of joint structures and exacerbation of knee symptoms and subsequent reduction of knee joint functions.

Obesity, generalized OA, malalignment and synovitis have consistently been reported as associated factors of progression in knee OA (62). Malalignment of the knee joint was found to be an independent risk factor for the progression of knee OA (63, 64). Varus and valgus malalignment increase the risk of medial and lateral osteoarthritis (OA) progression, respectively. This was shown in a systematic review of 14 studies (65).

A comparison of valgus versus valgus alignment compared with normal alignment showed that the association of varus alignment with progression was greater than valgus alignment. For every 1 degree change toward genu valgum, the annual rate of medial cartilage volume loss was reduced by 0.44%, whereas deformity towards varus alignment reduced the cartilage volume by 0.45% (66). The increased risk of alignment with knee OA progression is also dependent to weight and is especially greater in overweight and obese individuals but not in non-overweight persons. In addition, the impact of mechanical factors such as alignment varies by the status of joint injury. The less- damaged joint in mild OA may be less vulnerable to malalignment effects than the more-damaged joint in moderate OA (67). The odds of 18-month progression from baseline state in the medial compartment OA was 4.0. However, in K/L grade 2 knees, the odds was 2.0 whereas, in moderate OA (K/L grade 3) the odds was 10.0 (68). The rate of progression is greater in those with established radiographic abnormalities. The presence of joint space narrowing is a strong predictor of progression while osteophytes adds only a little of risk to it (69). Obesity

increases the risk of radiographic knee OA but has a lesser effect on disease progression. The risk of progression with obesity increases in patients with neutral or valgus alignment deformity (70). In patients with severe OA, high BMI does not cause progressive knee OA but in patient without joint space narrowing at onset, high BMI result in knee OA (62). Furthermore in OA with varus malalignment a $BMD \geq 30$ kg/m^2 increases the risk of OA development and progression. There is an association between obesity and hip or hand OA but the relation is weaker compared with knee OA. This implies that excess adipose tissue produces humoral factors and alters articular cartilage metabolism. It has been postulated that the leptin system could be a link between metabolic abnormalities and increased risk of OA (62). Quadriceps weakness is also an associated factor of knee OA progression which was observed only in women but not in men (71).

Subchondral bone marrow abnormalities determined by MRI which is an indication of knee OA was shown to be associated with the increased levels of collagen degradation markers. These markers are predictors of cartilage loss. In one study, subjects with low levels of cartilage oligomeric matrix protein (COMP) had lower cartilage volume loss whereas, higher levels of this marker was associated with greater cartilage loss. There was also a correlation between the level of this marker and the extent of bone marrow abnormalities diagnosed by MRI (72). These observations indicate potential for COMP in prediction of progressive OA disease and so it can be used for the identification of high risk individual (73). Furthermore, due to high sensitivity to changes, this marker can be used in the following treatment of OA (74, 75). Vitamin D deficiency was shown to be associated with knee OA and so low serum vitamin D can be considered as a risk factor of knee OA progression (37, 79).

Treatment

There is no cure for the treatment of OA and most treatments aimed to manage pain and movement restriction. Optimal management of patients with knee OA requires a combination of nonpharmacological and pharmacological modalities of therapy. Based on the available data, there is no statistically significant difference between nonpharmacological and pharmacological therapies (77).

The initial aim of treatment is often focused on alleviating the pain (table 2). Acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs) are often employed for the relief of mild to moderate pain. However, NSAIDs are typically more effective than acetaminophen but due to higher

complications of long term NSAIDs therapy, acetaminophen should be considered the first-line of therapy. In the absence of an adequate response or in case of more severe OA and presence of inflammation, alternative therapy should be considered. Long-term efficacy and safety of acetaminophen have been questioned recently. Combination of NSAIDs and acetaminophen may be used in conditions which neither of them alone are not sufficient for controlling pain or it is required to reduce NSAIDs dosages. COX-2 inhibitors are considered for patients who are at risk of gastrointestinal bleeding. However, these drugs are associated with increased risk of cardiovascular complications (77-79).

Acetaminophen is better yet to be taken regularly every day rather than as required, whereas, NSAIDs should be given at the lowest effective dosage for the shortest period of time. NSAIDs are superior to acetaminophen based on meta analysis of randomized clinical trials. The clinical response rate to NSAIDs as well as the proportion of patients who prefer taking NSAIDs was considerably greater than acetaminophen. However, NSAIDs are associated with more adverse effects than acetaminophen (79).

Topical NSAIDs provide efficacy similar to oral NSAIDs, but with far less systemic side effects. Cardiovascular, renal, and other serious adverse effects have not been reported by topical NSAIDs (80). Clinical trial data for these products have demonstrated efficacy superior to placebo or similar to oral diclofenac (77). Capsaicin cream derived from pepper plants is effective in managing pain and can exert further benefits as adjunctive and alternative to oral analgesic /anti-inflammatory agents. It is required to be regularly applied each day (77, 80).

Table 2. Nonpharmacological and pharmacological treatment recommended by the American College of Rheumatology for patients with osteoarthritis

- 1-Patients education
- 2-Weight reduction
- 3-Aerobic exercise
- 4-Physical therapy
- 5-Range-of-motion exercise
- 6-Muscle strengthening exercise
- 7- Assisted device for ambulation
- 8- Patellar tapping
- 9- Appropriate foot wear
- 10- Bracing
- 11- Occupational therapy
- 12- Joint protection and energy conservation.
- 13- Assisted devices for activities of daily living

Weight reduction

Patients with knee OA may be overweight and so should be encouraged to lose weight and maintain their weight at lower level. Meta-regression analysis showed that disability could be significantly improved when weight has been reduced over 5.1%, or at the rate of >0.24% reduction per week (81). Weight reduction is expected to modify the development of several conditions other than OA such as diabetes, hypertension, dyslipidemia which may be coexistent with OA and expected to be common among general population (82). However, progression of knee OA with varus alignment does not seem to be prevented by weight reduction (70).

Intraarticular therapy of knee OA.

Intraarticular corticosteroid therapy is usually used for treatment of knee OA. This type of treatment is especially recommended in patients who did not respond to acetaminophen and NSAIDs in particular is said to be effective in those patients who have joint effusion. Aspiration of synovial fluid and intraarticular injection of long-acting corticosteroid such as methylprednisolone, tramcinolone exert beneficial effects in relieving pain, improvement of function and preparing patients for continuing further treatment like physical therapy and participating in weight reduction programs. Several studies have shown a short period of benefits for six weeks or longer with intraarticular corticosteroid therapy compared with placebo (83- 85).

In a review of the literature, a short-term symptomatic relief was the only evidence-based benefit of corticosteroid injection in osteoarthritic knee. Accurate intraarticular placement was not achieved in up to 20% of injections which varied considerably with the anatomical approach used (85). In a study of twenty-eight trials (comprised of 1973 participants), the efficacy of intraarticular corticosteroid, intraarticular hyaluronan, and joint lavage, were compared. Intraarticular corticosteroid was more effective than placebo for pain reduction and patient global assessment in one week post injection. There was evidence of pain reduction between two to three weeks. In 4 to 24 weeks post injection, there was lack of evidence of effect on pain and function (77).

In general, the onset of effect was similar with intraarticular corticosteroid, but was less durable than with hyaluronan products. There was no difference between intraarticular corticosteroid and joint lavage. There was no difference between joint lavage and intraarticular

corticosteroid therapy regarding to efficacy, safety, and outcome measures (77). Injection of hyaluronate may be useful in patients with knee or hip OA. The onset of action is slow but benefits may persist for longer period compared with intraarticular corticosteroid

Experimental treatment

Statins can prevent cartilage matrix degradation and slow cartilage degeneration overtime. In animal models, treatment with statin significantly reduced the degeneration of articular cartilage, while in the control group, progressive cartilage degeneration developed over time.

Therefore, statins may be considered as a therapeutic agent for protection of cartilage against the progression of knee OA (86). Correction of serum vitamin D level is expected to exert protective effects against the development and worsening of knee OA especially in those with low BMD (76).

Physical therapy

Patients with symptomatic knee OA may benefit with physical therapy. Patients should be instructed appropriate exercise to reduce pain and improve functional capacity. In one study, physical therapy improved pain, physical function and WOMAC indices for short term period and even extended up to one year in a number of patients .However, in some studies, there was no difference in benefit compared with standard therapy (87- 89).

Using thermal modalities may be effective for relieving symptoms of knee OA. Cryotherapy may be administered by the application of ice packs or massage with ice. On the other hand, short term diathermy was not effective.

Glucosamine

Glucosamine and chondroitin sulfate have individually shown inconsistent efficacy in decreasing OA pain and improving joint function. Many studies confirmed OA pain relief with glucosamine and chondroitin sulfate use. However, the results of different studies are not consistent and so the data in this context should be regarded with caution before administration of glocosamine (90).

Large scale randomized controlled trials in more than 200 patients with osteoarthritis of the knee or hip that compared glucosamine, chondroitin, or their combination with placebo or head to head, demonstrated that glucosamine, chondroitin, and their combination do not reduce joint pain or have no impact on narrowing of joint space (91). In a double blind study of glucosamine/chondroitin versus placebo, after 2 years, the joint space

width loss in the placebo group was 0.166 mm which was not different from the treatment group. However, in mild knee OA (K/G grade 2) a trend toward improvement was observed compared with placebo group (92). In patients with symptomatic knee OA, these drugs may have structure-modifying effects with dosage of 1500 mg/day. In a few studies, treatment with glucosamine and /or chondroitin sulfate provided symptomatic benefit in patients with knee OA. However, treatment should be discontinued if no response was observed within six months.

Brace and footwear

Mild or moderate varus or valgus instability may be partly improved by using knee brace. Using valgus brace was shown to improve WOMAC scores (93). Knee braces and foot orthoses could be cautiously considered as conservative management for relief of pain and stiffness and improving physical function for persons with knee osteoarthritis (94). The results of previous studies suggest that knee braces and foot orthoses are effective in decreasing pain, joint stiffness, and drug dosage. They also improve proprioception, balance, Kellgren/Lawrence grading, and physical function scores in subjects with varus and valgus knee osteoarthritis. Using insoles can reduce pain and improve ambulation. Lateral wedged insoles can be of symptomatic benefit for some patients with medial tibiofemoral compartment OA.

Activities and exercises

Patients with knee OA should be encouraged to undertake regular aerobic walking exercise and muscle strengthening exercise and range of motion exercises. This may provide moderate improvement for both pain and quadriceps muscle strength. Patients with knee OA similar to healthy subjects can pursue physical activities to a level that does not increase the pain, provided that, the activity is not painful and does not predispose them to further trauma, higher levels of physical activities may also be permitted.

It should be considered that daily life activities as a risk factor for knee OA may increase the intensity and duration of pain. Nevertheless, engaging in regular recreational activities may be permitted for as long as they do not increase joint pain. In sedentary knee OA exercises and other structured activities have shown to exert favorable effect on pain (95).

Walking aids can reduce pain in patients with knee OA. Optimal use of a cane or crutch in the contralateral hand is being used in about 40% of patients with knee or hip OA.

Arthroscopic treatment

Randomized controlled trials of patients with joint space narrowing have shown that outcomes after arthroscopic lavage or debridement are no better than those after a sham procedure (placebo effect), and that arthroscopic surgery provides no additional benefit to physical and medical therapy. There is no evidence that removal of loose debris, cartilage flaps, torn meniscal fragments, and inflammatory enzymes have any pain relief or functional benefits in patients that have joint space narrowing on standing radiographs (96). Many patients with joint space narrowing are older with multiple medical comorbidities. When recommending arthroscopy to treat the painful osteoarthritic knee without mechanical symptoms, the consequences of arthroscopic treatment should be compared with clinical benefits expected to be conferred by such therapy (97).

Surgery

Knee OA should be initially treated conservatively, and surgery should be considered if knee symptoms have not been controlled despite adequate nonpharmacological and pharmacological therapy.

Surgical treatments for knee OA include arthroscopy, osteotomy and knee arthroplasty. Determining which of these procedures are most appropriate will depend on several factors, including the location and severity of OA damage, patient characteristics and risk factors.

The goal of osteotomy for unicompartmental knee OA is to transfer the weight load from the damaged compartment to undamaged areas, delaying the need for joint replacement. This procedure should be considered in young and active patients who are not suitable candidates for knee arthroplasty (77). In selected patients with isolated medial or patellofemoral OA, unicompartmental knee arthroplasty and patellofemoral replacement, respectively, can be successful (98, 99). Total knee arthroplasty relieves pain and improves quality of life for persons with advanced knee osteoarthritis. For patients with severe OA, total knee arthroplasty can be a safe, rewarding and cost-effective treatment.

In conclusion, knee OA is a frequent condition which predominately involves elderly population. Recognizing the risk factors and correction of associated factors of progression such as obesity, malalignment, vitamin D deficiency, and muscle weakness should be regarded as well. Regarding to irreversibility of OA damages and partial efficacy of available therapy, initiation of any treatment particularly medical treatment should be considered with

caution. Because most patients with knee OA are also affected with cardiovascular or renal underlying diseases which may be aggravated with OA medications.

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