

Temporomandibular Joint Osteoarthritis: Diagnosis and Long-Term Conservative Management: A Topic Review

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Abstract Degenerative joint disease (DJD), a common osteoarthritic problem encountered in clinical practice presents as a chronic debilitating disease resulting in altered joint structure due to degradation and loss of articular cartilage, along with changes in the subchondral bone and other soft tissues. DJD is a frequent finding in the Temporomandibular joints (TMJs). Consequently, a good understanding of the use of a diagnostic algorithm will lead to a better control of DJD in the TMJ. The etiopathogenesis of osteoarthritis is complex, and it is associated with

multiple risk factors. The condition progresses slowly through different phases with periods of remission and activity finally reaching the burnout phase. Conservative management forms the cornerstone for the treatment of most of these cases. This review attempts to acquaint the dentist with the diagnosis, pathogenesis and general characteristics of the disease while highlighting and updating them with the current conservative treatment algorithms in order to assist in the formulation of a treatment plan for these patients.

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Introduction

Osteoarthritis, a form of arthritis is characterized by chronic degeneration of the various hard and soft tissues around the joint [1, 2]. This results in anatomical changes in the joint, and joint pain due to alteration in peripheral and central pain processing mechanisms [2, 3]. Stress bearing joints of the body such as knee, hips, spine, and fingers are most commonly affected [4]. Osteoarthritis can also affect other joints in the body such as wrist, shoulder, ankle and Temporomandibular joint (TMJ). TMJ osteoarthritis affects the cartilage, subchondral bone, synovial membrane, and other hard and soft tissues causing changes such as TMJ remodeling, articular cartilage abrasion and deterioration [5, 6]. Osteoarthritis localized to the TMJ may also be a part of this generalized condition [7].

It is estimated that approximately 15 % of the world's population suffers from osteoarthritis [8]. Large scale multicenter, well conducted epidemiologic studies are

lacking in India. However, it is estimated that 22–29 % of people in India may have osteoarthritis [9].

Osteoarthritis can occur at any age, although, it occurs with greater frequency as age increases. At 40 years of age, only 20 % of the population may have osteoarthritis; however, by 65 years the rates drastically increase and a majority will exhibit radiographic evidence of the disease [10]. A study of subjects in the age group of 73–75 years estimated that 70 % of the subjects have radiographic evidence of osteoarthritis [11]. However, in spite of the high prevalence, only 9.6 % of men and 18 % of women ≥ 60 years have symptomatic Osteoarthritis. The prevalence pattern exhibits a bell shaped curve with peak prevalence in 5th and 6th decade followed by a reduction in the progression after 75 years [12, 13].

Epidemiologic studies on the prevalence of TMJ osteoarthritis vary due to variations in diagnostic criteria employed to define the condition. However, the prevalence and the symptomatic rates are similar to generalized osteoarthritis. In osteoarthritis of TMJ, clinical evidence of the disease occurs in 8–16 % of population [14, 15] TMJ Osteoarthritis may be unilateral or bilateral and has a strong preference for women [16]. This may be due to Estrogen Receptor alpha polymorphism and may be associated with increased pain susceptibility in female TMJ Osteoarthritis patients [17].

According to the American Academy of Orofacial Pain, TMJ Osteoarthritis is categorized into primary and secondary. Primary TMJ osteoarthritis is characterized by the absence of any distinct local or systemic factor. Secondary TMJ osteoarthritis is however associated with a previous traumatic event or disease [7].

Etiopathogenesis

Osteoarthritis has a complex and multifactorial etiology. Risk factors' include age, genetics, trauma (previous instances of fracture, repetitive adverse loading, high-impact and torsional loads, external or overt jaw trauma and instances of prolonged micro trauma), disturbances of joint or muscle (joint instability, inadequate muscle strength/endurance, internal derangements, disectomy, ligament laxity), systemic conditions (generalized osteoarthritis, infection and idiopathic degenerative process, congenital and developmental abnormality) [18–23].

The etiopathogenesis involves a sustained inflammatory process [4, 8, 24]. Metabolic or mechanical factors contribute to the early damage to the cartilage. This initiates a series of biomechanical changes in the hard and soft tissues of the joint triggering the immune response. Immune cells trigger an inflammatory response by releasing various

inflammatory mediators such as cytokines and chemokines. The process is coupled with the activation of the complement system, the release of cartilage degrading factors such as matrix metalloproteinase (MMPs) and prostaglandin E (PGE) which further damage the articular cartilage. This results in the eventual degradation and abrasion of joint cartilage and the remodeling of the subchondral bone by the initiation of a local inflammatory response [4, 23] (Fig. 1).

Clinical Features

In general, the natural course of TMJ osteoarthritis is favorable [26] and can be divided into three slow progressive phases, with periods of remission and cartilage regeneration [25, 27]. The initial stage where there is evolution of the condition is termed *early phase*. This may take on average 2.5–4 years. Clinically it is associated with clicking sounds and intermittent locking. The *intermediate phase*, associated with TMJ destruction, lasts on average 6 months to a year and clinically the patient may undergo spontaneous joint pain at rest or with function, limitation in opening, and grating sounds. The *late phase* is the stage at which there is no degenerative activity, and the joints are said to be stable or in the “burnout phase”. It lasts about 6 months, and it will eventually stabilize with time and therefore, if invasive procedures can be postponed with medical management, patients will ultimately benefit from it. There is the absence of joint pain, absence or presence of limitation, absence or presence of grating sounds. The entire process from initiation to the final burnout phase takes approximately 5.5 years [27].

The most common clinical signs and symptoms include pain, restriction in joint function, and joint sounds. Pain is usually dull aching and may have occasional sharp component on movement. Pain is prevalent in initial phases due to the presence of synovitis [25]. It may be associated with joint stiffness, limitation in mouth opening, increasing sensitivity to cold and damp and may be relieved with rest, and NSAIDs. Patients usually have morning stiffness for more than 30 min, joint crepitus, joint sounds and absence of joint warmth. Patients in advanced stages may exhibit facial skeletal remodeling, with chin deviation towards the affected side, unstable or fluctuating malocclusion with occlusal discrepancies [28]. Occlusal changes like skeletal anterior open bite, reduced overbite and increased overjet may be associated with osteoarthritic TMJ [23, 29]. In addition, internal derangements may co-exist in the same joint in approximately one-third of cases [11, 30].

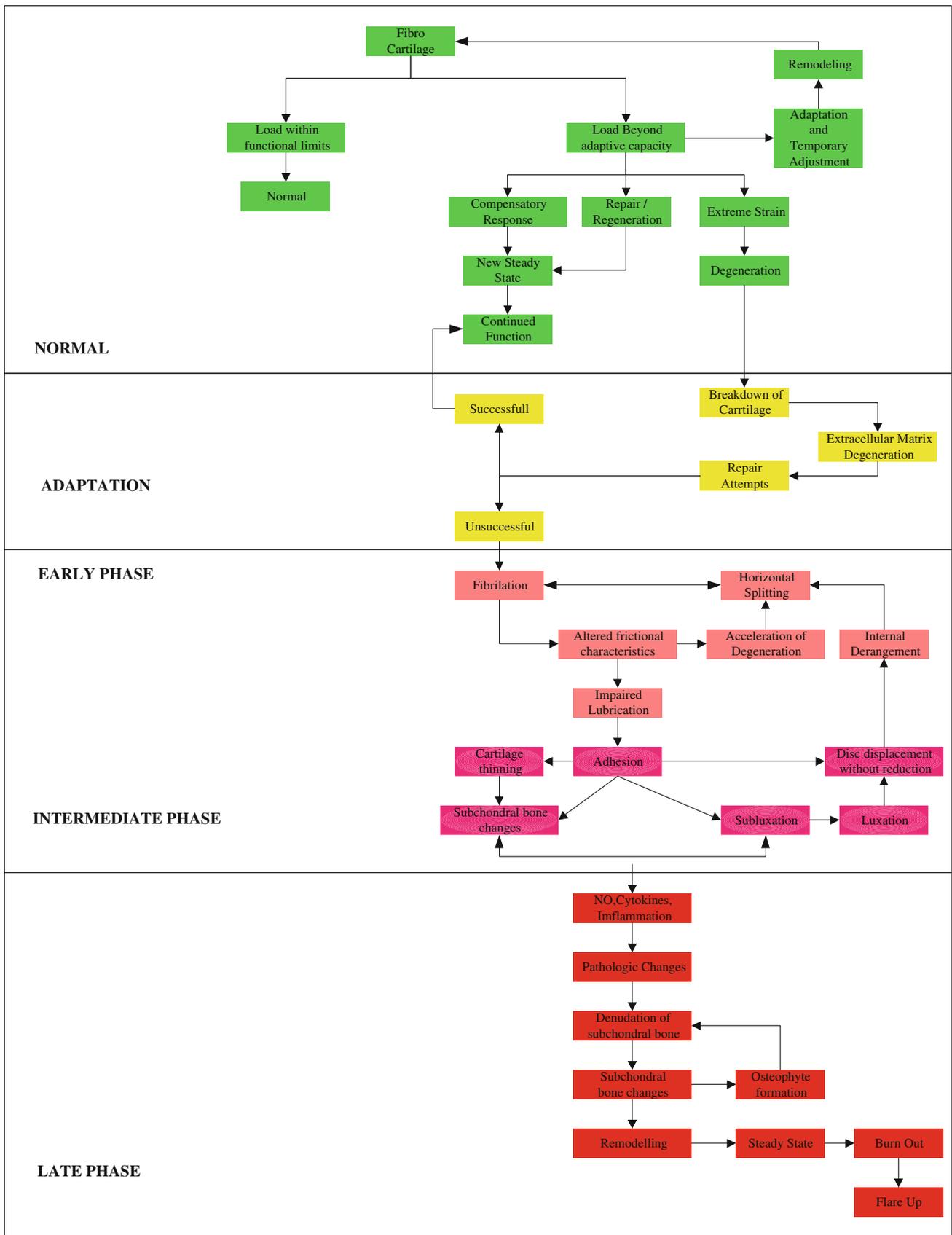


Fig. 1 Table showing the etiopathogenesis of TMJ osteoarthritis in the different phases



◀**Fig. 2** OPG of three cases of TMJ osteoarthritis. The condyles show typical OA changes namely flattening of the superior surface, loss of joint space of the affected joints, bird-beaking, generalized sclerosis of the articular surfaces and changes to the articular eminence as well

Diagnosis

The diagnosis starts with an orderly and systematic review of patient history and thorough physical examination. The information thus gained should be integrated with preliminary radiographic evidence to formulate a differential diagnosis. Once the clinician has a differential diagnosis, the diagnosis may be confirmed through appropriate imaging studies and necessary clinical lab studies. This entire process of completing the different aspects is essential for successful management of these patients.

Clinical Laboratory Evaluation and Imaging

In the lab panel, Erythrocyte sedimentation rate (ESR) is commonly used. Normal ESR should be 40 mm/h. Rheumatoid tests are used to rule out rheumatoid arthritis. Rheumatoid factor titer should be less than 1:40. The elevation in ESR and C reactive protein is indicative of an infectious or inflammatory etiology [4].

In addition, if radiographs are deemed necessary, the panoramic evaluation is the imaging of choice because it can be used as a screening tool to assess the overall status of the maxillo-mandibular complex (Fig. 2), and to rule out other possible disease processes. TMJ tomograms may be used for showing osseous condylar abnormalities in the clinic. However, transcranial projection examination is inferior [31]. Both transpharyngeal and transcranial views are no longer used for the radiographic diagnosis of TMJ osteoarthritis. A study comparing the different imaging modalities concluded that for the radiologic diagnosis of OA, reliability and marginal sensitivity was inadequate for panoramic radiography, average for MRI, and close to the threshold for excellent for CT. Using MRI, reliability was excellent for diagnosing disc displacements [32]. Cone beam CT, which reproduces multiple images including axial, coronal and sagittal planes of the joint, provides a comprehensive radiographic inspection of the bony components of the TMJ [31] (Fig. 3).

The following were the most frequent morphological changes observed: flattening of the anterior surface of the condyle; followed by erosions and irregularities of the joint surfaces; flattening of the articular surface of the temporal eminence, subchondral cysts, osteophytes; and idiopathic condyle resorption [33]. Ultrasonography has been tried because of its lower costs and has shown promising results [34].

Treatment

Once the diagnosis has been established; treatment will be contingent upon the stage of the disease clinical symptomatology, preexisting risk factors. Treatment of TMJ osteoarthritis should be directed at suppressing the active inflammatory process, preserving function, preventing further deformity and relieving pain [23]. Management is largely symptomatic. Studies have shown that nonsurgical treatment can successfully be used to treat patients with osteoarthritis [35]. Treatment includes physical therapy, pulsed electrical stimulation, pharmacological, topical ointments, supplements, steroid injections, hyaluronic acid (HA) injections, acupuncture. Early initiation of concomitant multimodal therapies offers best outcome for long term management [36] (Fig. 4).

Non Pharmacologic

Most of the recommendations for treatment of TMJ osteoarthritis are similar to algorithms followed for hip and knee osteoarthritis with certain changes. Recommendations include the use of education and self-management, regular telephone contact, referral to a physical therapist, muscle strengthening, appliances, thermal modalities, transcutaneous electrical nerve stimulation and acupuncture [37, 48]. There is moderate-quality evidence that acupuncture, transcutaneous electrical nerve stimulation, and low-level laser therapy reduce pain and that psychoeducational interventions improve psychological outcomes [38].

Patient education and self-management consist of patient counseling and patient education on the natural course of the disease. Activity modification includes patient instruction on soft diet, avoiding excessive mouth opening, avoiding gum chewing and habit modification. The use of active and passive jaw movement, manual therapy techniques, correction of body posture and relaxation techniques [23] have also been recommended. Thus a combined approach may be used in patients. Auto-massaging may help in reducing pain and stiffness but may not have any effect on range of motion [39].

Oral Appliance Therapy

Literature on the use of appliance therapy to treat osteoarthritis is weak since most of the studies lack the basis of sound clinical research. Certain studies on the use of appliances for reduction of painful conditions of TMJ have found resolution of painful symptoms after insertion of appliances [40–42]. Others conclude that they are not effective [43, 44]. Among appliances, joint stabilization appliances are most commonly used and they have been

hypothesized to provide joint stabilization, protect teeth, redistribute forces, relax elevator muscles, reduce bruxism decrease joint loading, and may secondarily stabilize occlusion and cause masticatory muscle relaxation [45]. In certain specific instances an anterior repositioning appliance may be beneficial [46]. The benefits of the splint therapy may be further enhanced in combination with pharmacotherapy [47]. In general, in carefully selected instances with an accurate diagnosis, patients report symptomatic relief of pain with the use of intra oral appliances. Therefore, intraoral appliance therapy cannot be ruled out for patients with TMJ arthropathies.

Irreversible Oral Rehabilitation

TMJ Osteoarthritis progresses through phases and finally reaches a burn out phase. Long term follow up of patients treated with conservative reversible procedures have shown best results [35, 63]. Dental procedures such as orthodontic treatment, full mouth rehabilitation and fixed partial dentures should be avoided in the active phase of the disease. In the active phase of the disease, reversible procedures and stabilization procedures must be carried out to offer best results.

Pharmacological

Pharmacological management is usually based on side effects, safety, patient acceptance, medical complexity, cost and routes of intake. Pharmacological modalities of treatment include acetaminophen, cyclooxygenase-2 (COX-2) non-selective and selective oral non-steroidal anti-inflammatory drugs (NSAIDs), topical NSAIDs and capsaicin, intra-articular injections of corticosteroids and hyaluronates, glucosamine and/or chondroitin sulphate for symptom relief; glucosamine sulphate, chondroitin sulphate and diacerein for possible structure-modifying effects and the use of opioid analgesics for the treatment of refractory pain [23, 37, 54].

Acetaminophen is one of the oldest and most widely used pharmacological agents for treatment of osteoarthritis. Although its effectiveness for pain reduction is not as high as NSAIDs it is preferred because of its safety profile and therefore, is the commonly used as the first line of treatment. Maximum dosage is up to 4 g/day. It should be used with caution in alcoholics and patients with history of liver problem.

NSAIDs are extremely beneficial for treating patients with TMJ Osteoarthritis as they have a dual effect of reducing pain and reducing inflammation. By reducing the inflammatory process we automatically slow down the

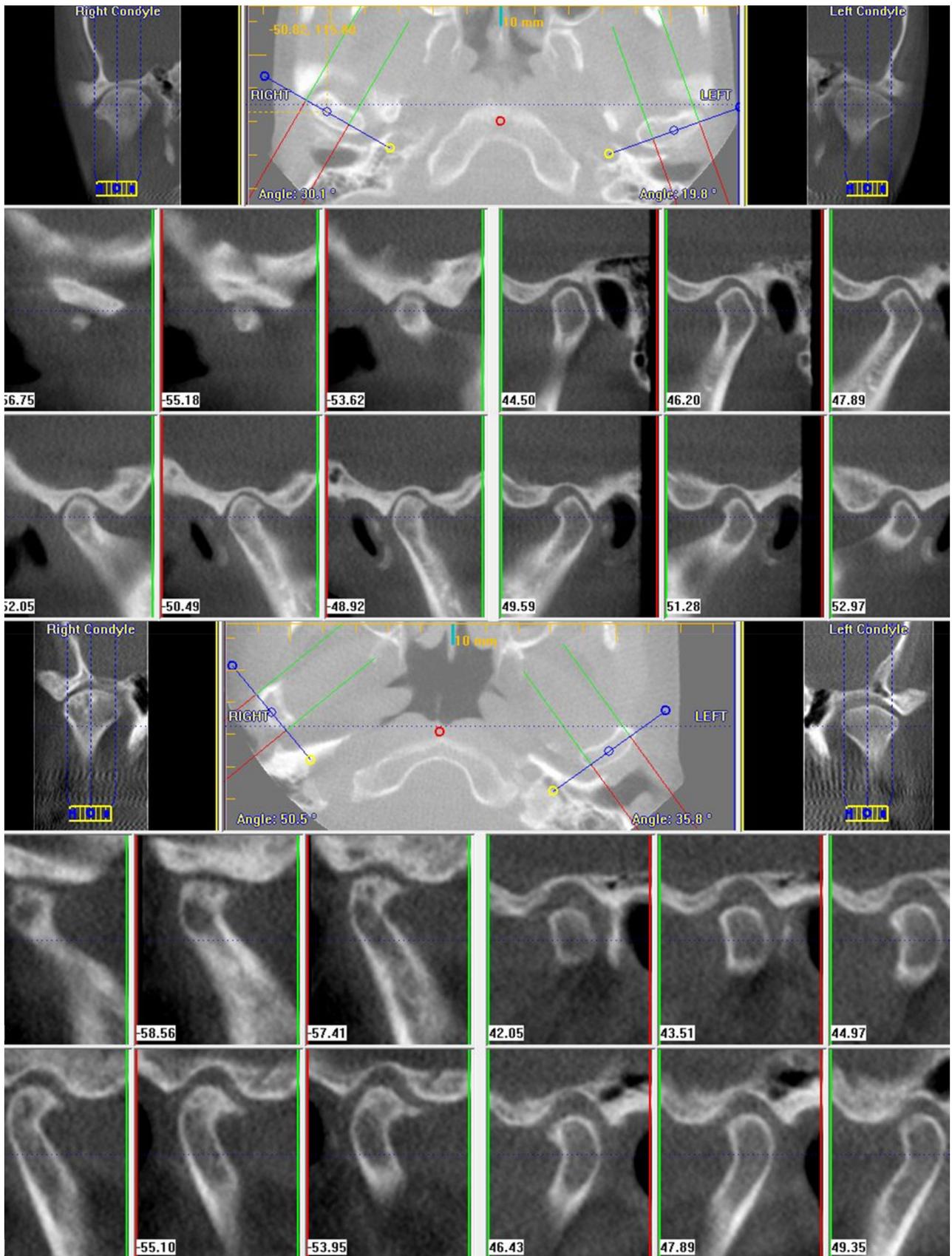


Fig. 3 TMJ coronal and sagittal views of two cases of TMJ osteoarthritis—one with unilateral involvement and other with bilateral TMJ OA. Both are taken with ICAT(R) CBCT machine and displayed with ICATvision software. The condyles show typical OA changes namely flattening of the superior surface, loss of joint space of the affected joints, bird-beaking and generalized sclerosis of the articular surfaces. Most commonly, there will be changes to the articular eminence as well

degenerative process. NSAIDs have the propensity to cause gastrointestinal (GI) problems and should be used with caution in patients with peptic ulcers and renal failure. Selective COX-2 inhibitors have a somewhat better GI profile. However, most of them were discontinued because of risk to cause Cerebrovascular accidents. In general NSAIDs can be used with GI prophylaxis (generally proton pump inhibitors).

Two randomized controlled trails indicate that tramadol is an effective and well tolerated as adjunctive therapy. In resistant cases, opioid analgesics can be used [48].

Supplements and Alternate Medicine

Ayurvedic medications have recently been compared to supplements and celecoxib and have shown similar efficacy. However, long term assessment and monitoring for side effects has to be done [49].

Supplements

These are perhaps the one of the controversial subjects in the management of OA.

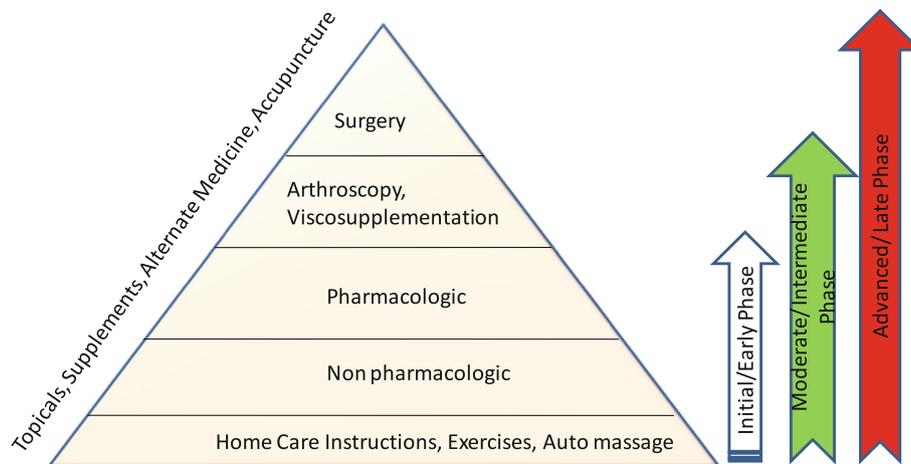
Among supplements glucosamine and chondroitin have been studied most with conflicting results. A meta-analysis in 2000 concluded that it may show some effects [50].

Glucosaminoglycan polysulfate and chondroitin sulfate have been suggested to have chondro-protective effects. Glucosamine in combination with hyaluronate reduced pain and improved joint function in one study [51]. However, another study concluded that it had no effect in comparison to placebo [52]. Other supplements that have been studied include vitamin D supplements and a recent study concluded that it may not have any effect [53]. Results of various studies have to be dealt with caution and more careful research is warranted in this area.

Topicals

Guidelines proposed by the American Academy of Orthopaedic Surgeons, European League Against Rheumatism, Osteoarthritis Research Society International, and National Institute for Health and Clinical Excellence for patients with mild to moderate osteoarthritis of the knee or hand, especially in instances of insufficient affected joints and/or a history of sensitivity to oral NSAID; topical NSAIDs may be considered before oral therapies [37]. Most of the clinical trials of topical NSAIDs, have studied diclofenac and ketoprofen, and these have shown improved safety and tolerability with the efficacy significantly superior to placebo and similar to oral NSAIDs (piroxicam being the exception). Diclofenac sodium topical solution 1.5 % with dimethyl sulfoxide was also found to be beneficial [55–57]. Topical salicylates and capsaicin have not shown substantial efficacy in clinical trials. In addition, concerns exist about their ability to cause serious adverse events such as unexpected poisonings with salicylates, capsaicin-induced nerve desensitization and its ability to increase the risk of skin ulcers in diabetic patients because of its autonomic nerve effects. Topicals trolamine salicylate [58] may be helpful.

Fig. 4 Treatment pyramid for TMJ Osteoarthritis



Intraarticular Injections, Arthrocentesis and Viscosupplementation

Intra-articular injection of local anesthetics and corticosteroids has also been suggested following failure to oral medications. Methylprednisolone and triamcinolone-acetonide have been used [4]. A systematic review concluded that lavage of the TMJ may be slightly more effective than nonsurgical treatment for pain reduction. However, this difference is not likely to be clinically relevant [59]. Systemic side effects include allergic reaction, elevated blood sugar in diabetics and long term effects include fat atrophy and cartilage softening.

Viscosupplementation is now gaining popularity. Viscosupplementation is effective in primary and secondary osteoarthritis [60]. Viscosupplementation has analgesic, anti inflammatory, anabolic, and chondroprotective effects [61]. It is a disease modifying agent as well as provides pain relief [62]. Arthrocentesis combined with HA injections may be useful in reducing pain, improving function. Controversy exists in the use of low molecular weight or high molecular weight HA.

A study which compared efficacy of six different treatment protocols providing TMJ arthrocentesis with or without additional drugs concluded that there was no significant difference regarding outcome with the different treatment protocols and different molecular weight HA: however, the five session low molecular weight HA was slightly better [64].

A systematic review on the use of HA injections suggests that since the superiority of HA injections have been shown only against placebo saline injections, their efficacy compared to other therapeutic modalities is inconclusive, and the outcomes may be comparable with those achieved with corticosteroid injections or oral appliances [65]. Hence, this approach should be used in select cases with failure of conservative techniques.

Surgery

Surgical interventions should be considered only when conservative modalities fail. The different surgical interventions include arthroplasty procedures such as condylectomy, autogenous disc replacement and total joint replacement procedures [66].

Future Prospects

The role of cytokine directed therapy might be an option in the future. TNF α and other proinflammatory cytokines have also been demonstrated to play an important role in

osteoarthritis [4, 23, 24]. Therefore, interventions directed at curtailing the activity of these proinflammatory cytokines may serve to reduce the destruction caused by these glycoproteins. Other potential future therapies include use of transforming growth factor beta 1, strontium ranelate, NGF antibodies, biological inhibitors of inflammatory cytokines, apoptosis (small molecule inhibitors of caspases), facilitation of cartilage repair using growth factors BMP-7, FGF-2, FGF-18, IGF-1, cartilage matrix using inhibitors of MMPs aggrecanases, cathepsins, etc. preventing oxidative damage utilizing antioxidants and enhancing lubrication, using agents such as lubricin, hyaluronan advanced glycation end-products inhibitors and selective estrogen receptor modulator like raloxifene (Ral) [67–72].

Stem cells are also one of the areas of research with promising results. Intra-articular injection of mesenchymal stem cells could delay the progression of TMJ osteoarthritis, and in vitro chondrogenic induction could enhance the therapeutic effects [73]. Efficacy of treatment and side effects have to be evaluated on long term basis.

Conclusion

Successful diagnosis is the key to management. The clinician should be able to recognize stages of osteoarthritis in order to provide contingent treatment. Treatment of advanced stage TMJ osteoarthritis can be successfully achieved by reversible and conservative non-surgical techniques. The first treatment option for the treatment of TMJ osteoarthritis should be conservative therapy owing to the non-progressive nature of the condition in the advanced stages. A conservative approach has a proven effective with the least morbidity to the patient. Irreversible oral rehabilitation should be avoided in active stages of the disease.

References

1. Lories RJ, Luyten FP (2011) Osteoarthritis as a whole joint disease. The bone-cartilage unit in osteoarthritis. *Nat Rev Rheumatol* 7:43–49
2. Poole AR (2012) Osteoarthritis as a whole joint disease. *HSS J* 8(1):4–6
3. Kidd B (2012) Mechanisms of pain in osteoarthritis. *HSS J* 8(1):26–28. doi:10.1007/s11420-011-9263-7
4. Jacofsky, David J, Anderson, Meredith L, Wolff III, Luther H (2005) Osteoarthritis Hospital Physician 41(7):17–25
5. Jiao K, Niu LN, Wang MQ, Dai J, Yu SB, Liu XD et al (2011) Subchondral bone loss following orthodontically induced cartilage degradation in the mandibular condyles of rats. *Bone* 48:362–371
6. Dijkgraaf LC, Liem RS, de Bont LG (1997) Ultrastructural characteristics of the synovial membrane in osteoarthritic temporomandibular joints. *J Oral Maxillofac Surg* 55(11):1269–1279

7. Reny de Leeuw, Gary D Klasser (eds) (2013) *Orofacial Pain: guidelines for assessment, diagnosis, and management* 5th edn. Quintessence Books
8. Egloff C, Hügler T, Valderrabano V (2012) Biomechanics and pathomechanisms of osteoarthritis. *Swiss Med Wkly* 19(142):w13583. doi:10.4414/sm.w.2012.13583
9. Chopra A, Patil J, Bilampelly V, Relwane J, Tandle H S (2001) Prevalence of rheumatic disease in rural population in Western India: a WHO-ILAR-COPCORD study. *J Assoc Physicians India* 49:240–246
10. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson DT, Giannini EH et al (1998) Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. *Arthritis Rheum* 41(5):778–799
11. Schmitter M, Essig M, Seneadza V, Balke Z, Schröder J, Rammelsberg P (2010) Prevalence of clinical and radiographic signs of osteoarthritis of the temporomandibular joint in an older persons community. *Dentomaxillofac Radiol*. doi:10.1259/dmfr/16270943
12. Bagge E, Bjelle A, Edén S, Svanborg A (1991) Osteoarthritis in the elderly: clinical and radiological findings in 79 and 85 year olds. *Ann Rheum Dis* 50(8):535–539
13. Bagge E, Bjelle A, Svanborg A (1992) Radiographic osteoarthritis in the elderly. a cohort comparison and a longitudinal study of the “70-year old people in Göteborg”. *Clin Rheumatol* 11(4):486–491
14. Toller PA (1973) Osteoarthritis of the mandibular condyle. *Br Dent J* 134(6):223–231
15. Mejersjö C (1987) Therapeutic and prognostic considerations in TMJ osteoarthritis: a literature review and a long-term study in 11 subjects. *Cranio* 5(1):69–78
16. Boyan BD, Tosi LL, Coutts RD, Enoka RM, Hart DA, Nicoletta DP et al (2013) Addressing the gaps: sex differences in osteoarthritis of the knee. *Biol Sex Differ*. doi:10.1186/2042-6410-4-4
17. Kang SC, Lee DG, Choi JH, Kim ST, Kim YK, Ahn HJ (2007) Association between estrogen receptor polymorphism and pain susceptibility in female temporomandibular joint osteoarthritis patients. *Int J Oral Maxillofac Surg* 36(5):391–394
18. Buckwalter JA, Mankin HJ (1998) Articular cartilage: degeneration and osteoarthritis, repair, regeneration, and transplantation. *Instr Course Lect* 47:487–504
19. Ricks ML, Farrell JT, Falk DJ, Holt DW, Rees M, Carr J et al (2013) Osteoarthritis in temporomandibular joint of Col2a1 mutant mice. *Arch Oral Biol*. doi:10.1016/j.archoralbio.2013.02.008
20. Boyce MK, Trumble TN, Carlson CS, Groschen DM, Merritt KA, Brown MP (2013) Non-terminal animal model of post-traumatic osteoarthritis induced by acute joint injury. *Osteoarthritis Cartilage*. doi:10.1016/j.joca.2013.02.653
21. Buckwalter JA (2012) The role of mechanical forces in the initiation and progression of osteoarthritis. *HSS J* 8(1):37–38
22. Xu L, Polur I, Lim C, Servais JM, Dobeck J, Li Y, Olsen BR (2009) Early-onset osteoarthritis of mouse temporomandibular joint induced by partial disectomy. *Osteoarthritis Cartilage*. doi:10.1016/j.joca.2009.01.002
23. Tanaka E, Detamore MS, Mercuri LG (2008) Degenerative disorders of the temporomandibular joint: etiology, diagnosis, and treatment. *J Dent Res* 87(4):296–307
24. Wang XD, Kou XX, Mao JJ, Gan YH, Zhou YH (2012) Sustained inflammation induces degeneration of the temporomandibular joint. *J Dent Res*. doi:10.1177/0022034512441946
25. Wang XD, Kou XX, He DQ, Zeng MM, Meng Z, Bi RY, Liu Y et al (2012) Progression of cartilage degradation, bone resorption and pain in rat temporomandibular joint osteoarthritis induced by injection of iodoacetate. *PLoS One*. doi:10.1371/journal.pone.0045036
26. Manfredini D, Favero L, Gregorini G, Cocilovo F, Guarda-Nardini L (2013) Natural course of temporomandibular disorders with low pain-related impairment: a 2-to-3-year follow-up study. *J Oral Rehabil*. doi:10.1111/joor.12047
27. Stegenga B, de Bont LG, Boering G, van Willigen JD (1991) Tissue responses to degenerative changes in the temporomandibular joint: a review. *J Oral Maxillofac Surg* 49(10):1079–1088
28. Chen YJ, Shih TT, Wang JS, Wang HY, Shiau YY (2005) Magnetic resonance images of the temporomandibular joints of patients with acquired open bite. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 99(6):734–742
29. Schellhas KP, Piper MA, Omlie MR (1992) Facial skeleton remodeling due to temporomandibular joint degeneration: an imaging study of 100 patients. *Cranio* 10(3):248–259
30. Dimitroulis G (2005) The prevalence of osteoarthritis in cases of advanced internal derangement of the temporomandibular joint: a clinical, surgical and histological study. *Int J Oral Maxillofac Surg* 34(4):345–349
31. Meng JH, Zhang WL, Liu DG, Zhao YP, Ma XC (2007) Diagnostic evaluation of the temporomandibular joint osteoarthritis using cone beam computed tomography compared with conventional radiographic technology. *Beijing Da Xue Xue Bao* 39(1):26–29
32. Ahmad M, Hollender L, Anderson Q, Kartha K, Ohrbach R, Truelove EL, John MT et al (2009) Research diagnostic criteria for temporomandibular disorders (RDC/TMD): development of image analysis criteria and examiner reliability for image analysis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. doi:10.1016/j.tripleo.2009.02.023
33. Nah KS (2012) Condylar bony changes in patients with temporomandibular disorders: a CBCT study. *Imaging Sci Dent*. doi:10.5624/isd.2012.42.4.249
34. Landes C, Walendzik H, Klein C (2000) Sonography of the temporomandibular joint from 60 examinations and comparison with MRI and axiography. *Sonography J Craniomaxillofac Surg* 28(6):352–361
35. de Leeuw R, Boering G, Stegenga B, de Bont LG (1995) Symptoms of temporomandibular joint osteoarthritis and internal derangement 30 years after non-surgical treatment. *Cranio* 13(2):81–88
36. Langworthy MJ, Saad A, Langworthy NM (2010) Conservative treatment modalities and outcomes for osteoarthritis: the concomitant pyramid of treatment. *Phys Sportsmed* 38(2):133–145
37. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N et al (2008) OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage* 16(2):137–162
38. Jamtvedt G, Dahm KT, Christie A, Moe RH, Haavardsholm E, Holm I, Hagen KB (2008) Physical therapy interventions for patients with osteoarthritis of the knee: an overview of systematic reviews. *Phys Ther* 88(1):123–136
39. Atkins DV, Eichler DA (2013) The effects of self-massage on osteoarthritis of the knee: a randomized, controlled trial. *Int J Ther Massage Bodywork* 6(1):4–14
40. Wahlund K, List T, Larsson B (2003) Treatment of temporomandibular disorders among adolescents: a comparison between occlusal appliance, relaxation training, and brief information. *Acta Odontol Scand* 61:203–211
41. Tanaka EE, Arita ES, Shibayama B (2004) Occlusal stabilization appliance: evaluation of its efficacy in the treatment of temporomandibular disorders. *J Appl Oral Sci* 12(3):238–243
42. Pandis N (2011) Modest improvement in temporomandibular disorder-related pain associated with use of hard stabilization appliances compared with use of non occluding appliances or no therapy. *J Am Dent Assoc* 142(11):1295–1296

43. Nemcovsky CE, Gazit E, Serfati V, Gross MA (1992) Comparative study of three therapeutic modalities in a temporomandibular disorder (TMD) population. *Cranio* 10(2):148–155
44. Niemelä K, Korpela M, Raustia A, Ylöstalo P, Sipilä K (2012) Efficacy of stabilisation splint treatment on temporomandibular disorders. *J Oral Rehabil*. doi:10.1111/j.1365-2842.2012.02335.x
45. Stegenga B, Dijkstra PU, de Bont LG, Boering G (1990) Temporomandibular jointosteoarthritis and internal derangement. Part II: Additional treatment options. *Int Dent J* 40(6):347–353
46. Madani AS, Mirmortazavi A (2011) Comparison of three treatment options for painful temporomandibular joint clicking. *J Oral Sci* 53(3):349–354
47. Inchingolo F, Tatullo M, Marrelli M, Inchingolo AM, Tarullo A et al (2011) Combined occlusal and pharmacological therapy in the treatment of temporo-mandibular disorders. *Eur Rev Med Pharmacol Sci* 15(11):1296–1300
48. Sinusas Keith (2012) Osteoarthritis: diagnosis and treatment. *Am Fam Physician* 85(1):49–56
49. Chopra A, Saluja M, Tillu G, Sarmukkaddam S, Venugopalan A, Narsimulu G et al (2013) Ayurvedic medicine offers a good alternative to glucosamine and celecoxib in the treatment of symptomatic knee osteoarthritis: a randomized, double-blind, controlled equivalence drug trial. *Rheumatology (Oxford)*. doi:10.1093/rheumatology/kes414
50. McAlindon TE, LaValley MP, Gulin JP, Felson DT (2000) Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis. *JAMA* 283(11):1469–1475
51. Li C, Jia Y, Zhang Q, Shi Z, Chen H (2011) Glucosamine hydrochloride combined with hyaluronate for temporomandibular joint osteoarthritis: a primary report of randomized controlled trial. *Hua Xi Kou Qiang Yi Xue Za Zhi* 29(6):632–635, 639
52. Cahlin BJ, Dahlström L (2011) No effect of glucosamine sulfate on osteoarthritis in the temporomandibular joints—a randomized, controlled, short-term study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. doi:10.1016/j.tripleo.2011.06.012
53. McAlindon T, LaValley M, Schneider E, Nuite M, Lee JY, Price LL, Lo G et al (2013) Effect of vitamin D supplementation on progression of knee pain and cartilage volume loss in patients with symptomatic osteoarthritis: a randomized controlled trial. *JAMA*. doi:10.1001/jama.2012.164487
54. Blumstein H, Gorevic PD. (2005) Rheumatologic illnesses: treatment strategies for older adults. *Geriatrics*. 60(6):28–35. Review
55. Argoff CE (2013) Topical analgesics in the management of acute and chronic pain. *Mayo Clin Proc*. doi:10.1016/j.mayocp.2012.11.015
56. Roth SH, F. P. (n.d.). (2011) Diclofenac sodium topical solution 1.5 % w/w with dimethyl sulfoxide compared with placebo for the treatment of osteoarthritis: pooled safety results. *Postgrad Med*. 123(6):180–8
57. Barthel HR, Axford-Gatley RA (2010) Topical nonsteroidal anti-inflammatory drugs for osteoarthritis. *Postgrad Med*. doi:10.3810/pgm.2010.11.2227
58. Rothacker DQ, Lee I, Littlejohn TW 3rd (1998) Effectiveness of a single topical application of 10% trolamine salicylate cream in the symptomatic treatment of osteoarthritis. *J Clin Rheumatol*. 4(1):6–12
59. Vos LM, Huddleston Slater JJ, Stegenga B (2013) Lavage therapy versus nonsurgical therapy for the treatment of arthralgia of the temporomandibular joint: a systematic review of randomized controlled trials. *J Orofac Pain*. doi:10.11607/jop.1007
60. Święchowicz S, Ostałowska A, Kasperczyk A, Nowak D, Birkner E, Kasperczyk S (2012) Evaluation of hyaluronic acid intra-articular injections in the treatment of primary and secondary osteoarthritis of the knee. *Pol Orthop Traumatol* 22(77):105–109
61. Axe JM, Snyder-Mackler L, Axe MJ (2013) The role of viscosupplementation. *Sports Med Arthrosc*. doi:10.1097/JSA.0b013e3182673241
62. Clegg TE, Caborn D, Mauffrey C (2013) Viscosupplementation with hyaluronic acid in the treatment for cartilage lesions: a review of current evidence and future directions. *Eur J Orthop Surg Traumatol*. doi:10.1007/s00590-012-0940-0
63. deLeeuw R, Boering G, Stegenga B, de Bont LG (1995) Radiographic signs of temporomandibular joint osteoarthritis and internal derangement 30 years after nonsurgical treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 79(3):382–392
64. Manfredini D, Rancitelli D, Ferronato G, Guarda-Nardini L (2012) Arthrocentesis with or without additional drugs in temporomandibular joint inflammatory-degenerative disease: comparison of six treatment protocols*. *J Oral Rehabil*. doi:10.1111/j.1365-2842.2011.02265.x
65. Manfredini D, Piccotti F, Guarda-Nardini L (2010) Hyaluronic acid in the treatment of TMJ disorders: a systematic review of the literature. *Cranio* 28(3):166–176
66. Editors: Daniel M. Laskin, Charles S. Greene, William L. Hylander (2006) *Temporomandibular disorders: an evidenced-based approach to diagnosis and treatment*
67. Ying B, Chen K, Hu J, Man C, Feng G, Zhang B, Zhu S (2012) Effect of different doses of transforming growth factor-β(1) on cartilage and subchondral bone in osteoarthritic temporomandibular joints. *Br J Oral Maxillofac Surg*. doi:10.1016/j.bjoms.2012.05.014
68. Zhang B, Hu J, Man C, Zhu S (2011) Effect of intra-articular administration of interleukin 1 receptor antagonist on cartilage repair in temporomandibular joint. *J Craniofac Surg*. doi:10.1097/SCS.0b013e31820873c6
69. Lotz MK, Kraus VB (2010) New developments in osteoarthritis. posttraumatic osteoarthritis: pathogenesis and pharmacological treatment options. *Arthritis Res Ther* 12(3):211
70. Man C, Zhu S, Zhang B, Hu J (2009) Protection of articular cartilage from degeneration by injection of transforming growth factor-beta in temporomandibular joint osteoarthritis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 108(3):335–340
71. Kavas A, Cagatay ST, Banerjee S, Keskin D, Tezcaner A (2013) Potential of Raloxifene in reversing osteoarthritis-like alterations in rat chondrocytes: an in vitro model study. *J Biosci* 38(1): 135–147
72. Garg S, Syngle A, Vohra K (2013) Efficacy and tolerability of advanced glycation end-products inhibitor in osteoarthritis: a randomized, double-blind, placebo-controlled study. *Clin J Pain*. doi:10.1097/AJP.0b013e318272ebec
73. Chen K, Man C, Zhang B, Hu J, Zhu SS (2013) Effect of in vitro chondrogenic differentiation of autologous mesenchymal stem cells on cartilage and subchondral cancellous bone repair in osteoarthritis of temporomandibular joint. *Int J Oral Maxillofac Surg*. doi:10.1016/j.ijom.2012.05.030