

MOBILITY

JOURNAL



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CONTENTS

SECTION 1**REVIEW ARTICLE**

- Osteoarthritis: New concepts in nutraceuticals 4

SECTION 2**REVIEW ARTICLE**

- Role of vitamin D and calcium in bone health 6

SECTION 3**JOURNAL SCAN**

- Undenatured type II collagen supplement in knee osteoarthritis 7
- Role of polymer hyaluronic acid in knee osteoarthritis 8

SECTION 4**CONFERENCE UPDATE**

- Role of biomechanical factors in clinical versus structural progression of knee OA 8
- Factors associated with obesity-induced changes in osteoarthritis progression 9

SECTION 5**GLOBAL NEWS**

- Anti-inflammatory effect of curcumin in osteoarthritis 9

SECTION 6**X-RAY INTERPRETATION**

- Arthroscopy 10
- Arthroplasty 11
- Trauma 13

CONFERENCE CALENDAR

Osteoarthritis: New concepts in nutraceuticals

OVERVIEW

Osteoarthritis (OA), the most common form of arthritis is a degenerative disease and a major cause of pain and disability in older adults. It is characterized by cartilage and synovium inflammation which causes joint stiffness, swelling, pain, and loss of mobility.^{1,2} OA weakens the structure and functionality of joint cartilage as a result of an imbalance between anabolic and catabolic processes in the cartilage tissue resulting in its degradation. Nutraceuticals are dietary compounds that play a pivotal role in the balance of such processes within articular cartilage.²

Various available nutraceuticals are fish oil, glycosaminoglycans (GAGs) such as hyaluronic acid, olive oil, undenatured type II collagen (UC-II) and botanical extracts such as curcumin.²

UNDENATURED TYPE II COLLAGEN

- Cartilage is a complex tissue which is composed of an extensive extracellular matrix of water, type II collagen and aggrecan surrounding the cellular component³
- Collagen type II is the main structural component of collagen tissue and extracellular matrix protein in hyaline articular cartilage.^{4,5} Degradation products of this protein in urine are associated with the progression of articular damage in osteoarthritis⁴
- Undenatured type II collagen (UC-II) is a nutritional supplement derived from chicken sternum cartilage which supports healthy joints^{2,6}
- UC-II reduces circulating levels of inflammatory cytokines, thereby reducing both the incidence and the severity of OA⁶
- Therefore, it is recommended to prevent joint destruction, pain and loss of function by its mechanism of oral tolerance that avoids T-cells attack to collagen fibres in joints.⁴

A study showed potential efficacy of undenatured type II collagen in knee osteoarthritis owing to benefit in alleviating the joint pain

Clinical evidence

- A randomized, double blind, placebo controlled study⁶ was conducted among healthy subjects having knee pain with physical activity to understand the efficacy and tolerability of UC-II in moderating joint function and joint pain
- Subjects were randomized to receive placebo or UC-II (40 mg daily) for 120 days
- In the UC-II group, a statistically significant improvement was seen in average knee extension compared to placebo ($81.0 \pm 1.3^\circ$ vs $74.0 \pm 2.2^\circ$; $p = 0.011$) and to baseline ($81.0 \pm 1.3^\circ$ vs $73.2 \pm 1.9^\circ$; $p = 0.002$). Also, a statistically significant change in average knee extension at day 90 ($78.8 \pm 1.9^\circ$ vs $73.2 \pm 1.9^\circ$; $p = 0.045$) versus baseline was seen in UC-II group
- It was also noted that the UC-II group exercised longer before experiencing any initial joint discomfort at day 120 (2.8 ± 0.5 min, $p = 0.019$), compared to baseline (1.4 ± 0.2 min). Also, five individuals in the UC-II cohort had no pain during or after the stepmill protocol ($p = 0.031$, within visit) as compared to one subject in the placebo group
- It was concluded that daily supplementation with 40 mg of UC-II led to improved knee joint extension in healthy subjects and it was well tolerated
- The results of this study highlight the potential efficacy of undenatured type II collagen in knee osteoarthritis owing to benefit in alleviating the joint pain.

HYALURONIC ACID

- GAGs are basic components of the extracellular matrix and synovial fluid. Hyaluronic acid (HA), a GAG, improves the mechanical properties of the synovial fluid and has a biochemical regulatory role on joint tissue.²
- HA is a newer approach in effectively reducing the side effects of OA.⁷ Mobilee is a type of HA extracted from rooster comb.^{8,9} Its effectiveness is due to utilization of its actions like lubrication, anti-inflammatory and chondroprotective effects⁷
- Oral HA binds to toll-like receptor-4 (TLR-4) and enhances the production of interleukin-10 (IL-10) and cytokine signaling, which leads to anti-inflammation of arthritis⁷
- HA is accountable for the viscoelastic properties of synovial fluid, which contains lower concentration and molecular weight (MW) of HA in osteoarthritic joints than in healthy ones. Thus, the goal of intra-articular therapy with HA is to help replace synovial fluid that has lost its viscoelastic properties.¹⁰

Clinical evidence

In a study¹¹ done in patients with OA, daily treatment with oral HA preparations resulted in significant improvements of scores including Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), visual analogue scales (VAS), Japanese Knee Osteoarthritis Measure (JKOM) and SF-36v2 after 1-4 months. The results with oral HA products for the treatment of mild to moderate knee OA were promising and in line with the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) recommendation to use symptomatic slow-acting drugs for osteoarthritis (SYSADOA).¹¹

CURCUMIN

- Curcumin is an aromatic molecule having anti-arthritis effects in humans with OA and rheumatoid arthritis (RA). These beneficial effects of curcuminoids in OA are because of local anti-inflammatory effects rather than systemic effects¹²
- The anti-inflammatory effects can be accounted to inhibition of the activity of COX-2 and 5-LOX enzyme, thereby protecting chondrocytes from the negative effects of IL-1 β .²

Clinical evidence

- A meta-analysis¹³ of randomized clinical trials (RCTs) of turmeric extracts and curcumin including 29 articles was done to evaluate the efficacy of curcuma for reducing the symptoms of arthritis
- A pain visual analogue score (PVAS) and WOMAC were used for the major outcomes of arthritis. Three among the included RCTs showed reduction of PVAS (mean difference: -2.04 [-2.85, -1.24]) with turmeric/curcumin in comparison with placebo ($p < 0.00001$), whereas meta-analysis of four studies showed a decrease of WOMAC with turmeric/curcumin treatment (mean difference: -15.36 [-26.9, -3.77]; $p = 0.009$). The results supported the efficacy of turmeric extract (about 1000 mg/day of curcumin) in the treatment of arthritis.¹³

CONCLUSION

OA is a degenerative disease characterized by cartilage and synovium inflammation. Nutraceuticals are dietary compounds which are incorporated in daily diet due to their ease of availability such as fish oil, curcumin found in turmeric, hyaluronic acid and UC-II to regulate the balance between anabolic and catabolic processes in joint tissue, thereby helping in prevention and management of OA.

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Role of vitamin D and calcium in bone health

OVERVIEW

Calcium is the most abundantly stored element and a key nutrient in the human body. Approximately, 99% of it is stored in the bones and teeth, with only less than 1% stored in extracellular serum.¹ Its metabolism is regulated by the parathyroid hormone (PTH)–vitamin D endocrine system. The rapid release of mineral from the bone is essential to maintain adequate levels of ionized calcium in serum. It is absorbed by active transport and by passive diffusion across the intestinal mucosa. Its active transport is dependent on the action of calcitriol and the intestinal vitamin D receptor (VDR).² Vitamin D stimulates intestinal calcium and phosphorus absorption along with bone calcium mobilization. It also increases renal reabsorption of calcium in the distal tubule.³ It supports bone growth and mineralization by osteoblasts and osteoclasts.^{4,5} Vitamin D deficiencies are ameliorated with the infusion of calcium in appropriate amounts, therefore, calcium and vitamin D act synergistically on bone.⁶

CLINICAL SIGNIFICANCE

- Calcium, being an essential component of bone health can result in bone density changes in elderly if not taken in adequate amount.¹ This reduction in bone mass and structural deterioration results in osteoporotic fractures in elderly people. Calcium plus vitamin D supplementation is recommended for the prevention of osteoporosis and subsequent fractures. Available data shows that supplementation could decrease the risk of total and hip fractures by 15 and 30%, respectively⁵
- Vitamin D, a non-polar lipid has poor bioavailability because of its low solubility in aqueous fluids of the gastrointestinal tract (GIT). Micellisation process disperses fatty molecules into aqueous micellar spheres and enables better absorption
- Nanotechnology-based nanoemulsion formulation of vitamin D3 ($d < 200$ nm) are superior to the conventional

Available data shows that supplementation of calcium + vitamin D could decrease the risk of total and hip fractures by 15 and 30%, respectively

coarse emulsions ($d > 200$ nm) in terms of bioavailability and homogeneity based on simulated GIT system⁷

- » In order to test this, a first ever randomized trial⁷ was conducted which included 180 healthy adults. These were randomized to receive either micellised (DePura, group A) or conventional vitamin D3 (Calcirol, group B) at a monthly dose of 60,000 IU (1500 µg) for 6 months
- » The end points were serum 25-hydroxyvitamin D (25(OH)D), parathyroid hormone (PTH), Ca, phosphate, alkaline phosphatase and urinary Ca:creatinine ratio
- » The findings were: In both groups, there was a significant increase in serum 25(OH)D levels following supplementation [group A: 21.5 to 76.7 nmol/l ($p < 0.001$); group B: 22.8 to 57.8 nmol/l ($p < 0.001$)]. However, in micellised group, there was an additional increase of 20.2 nmol/l in serum 25(OH)D levels ($p < 0.001$). The difference between the groups was 17.5 nmol/l, which remained statistically significant ($p < 0.001$)
- » Serum PTH was significantly lowered in both groups, thereby reducing the risk of bone loss and fractures in older people. No hypercalcaemia or hypercalciuria was seen
- » Thus, supplementation with both micellised and conventional vitamin D3 was safe and resulted in significant rise in serum 25(OH)D levels. However, micellised vitamin D3 formulation was more effective in achieving higher level of serum 25(OH)D.

CONCLUSION

Vitamin D and calcium work synergistically on bone and hence, their supplementation is required for prevention of fractures. Vitamin D supports bone growth and its deficiency leads to decreased serum 25(OH) D levels. Micellised vitamin D3 supplementation helps in achieving higher levels of 25(OH) D and lower serum PTH, thereby reducing risk of fractures.

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SECTION 3

JOURNAL SCAN

Undenatured type II collagen supplement in knee osteoarthritis

Osteoarthritis is the most common form of arthritis associated with destruction of joint cartilage and remodeling of the adjacent bone. The pharmacotherapy of OA includes various over the counter analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), intra-articular injections of corticosteroids, plus tramadol and other opioid analgesics to relieve severe pain. Although these agents help in pain relief, they have been ineffective in managing the underlying progression of OA. Therefore, additional agents which help in preventing the progression of OA and improve its symptoms are considered to be essential.

Undenatured type II collagen (UC-II) is a nutritional supplement derived from chicken sternum cartilage. It protects against the onset of joint damage in OA due to the induction and migration of T-regulatory cell to the area of inflammation and damage. Also, T-regulatory cells produce anti-inflammatory cytokines that stimulate chondrocytes to synthesize cartilage matrix components. It is, therefore, a therapeutic alternative for treatment of OA.

- A randomized, double-blind, placebo-controlled study was conducted in OA patients to evaluate the efficacy and tolerability of UC-II in improving knee symptoms. It was compared to placebo and glucosamine hydrochloride plus chondroitin sulfate (GC). 191 volunteers, randomized into three groups received a daily dose of UC-II (40 mg), GC (1500 mg G & 1200 mg C), or placebo for a 180-day period. Change in total Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) from baseline through

Undenatured type II collagen (UC-II) protects against the onset of joint damage in OA through an integrated molecular mechanism

day 180 for the UC-II group versus placebo and GC were taken as primary endpoints. Secondary endpoints included the Lequesne Functional Index (LFI), the Visual Analog Scale (VAS) for pain and the WOMAC subscales. The observations were:

- UC-II group showed a significant reduction in overall WOMAC score compared to placebo ($p=0.002$). UC-II also resulted in significant changes for all three WOMAC subscales: pain ($p=0.0003$ vs. placebo); stiffness ($p=0.004$ vs. placebo); physical function ($p=0.007$ vs. placebo)
- There was a significant decrease in mean VAS score at day 180 in UC-II supplement group versus both placebo (22.6 vs. 17.0; 95 % $p=0.002$). A significant reduction was seen in LFI score as well with UC-II supplement.

Thus, the study established the efficacy and tolerability of UC-II which is a nutritional ingredient in significantly improving knee function in OA subjects as compared to placebo.

Source: Lugo JP, Saiyed ZM, Lane NE. Efficacy and tolerability of an undenatured type II collagen supplement in modulating knee osteoarthritis symptoms: a multicenter randomized, double-blind, placebo-controlled study. *Nutr J.* 2016;15:14.

Role of polymer hyaluronic acid in knee osteoarthritis

Osteoarthritis of knee joints is a highly prevalent disease associated with significant disability. Therefore, with age, the risk of OA in knee joints increases. This calls for treatment options which are effective and well-tolerated,

Hyaluronic acid (HA), a mucopolysaccharide is present in synovial fluid. Intra-articular administration of HA helps in relieving symptoms associated with knee OA. Since it needs to be administered repeatedly requiring multiple injections in the joint cavity, it becomes a major drawback of the therapy. With an increase in demand for effective and less complicated treatment options, oral administration of HA is desirable to relieve symptoms of knee OA. Orally administered HA is absorbed and distributed to the knee joints while retaining its biological activities. HA binds to TLR4 increasing the secretion of suppressor of cytokine signalling 3 (SOCS3), thereby suppressing proinflammatory cytokine expression. This binding also suppresses the expression of pleiotrophin; hence, suppressing inflammation.

A prospective, randomized, double-blind, placebo-controlled study evaluated the efficacy of orally administered HA for symptom relief in older adults with knee OA. The study was conducted over a period of one year with 200mg of HA administered orally. 60 patients aged >50 years with Kellgren-Lawrence (K/L) grade 2 or grade 3 were randomized to receive either 4 capsules each of 50 mg HA or 4 capsules of cornstarch

over a period of 12 months. Japanese Knee Osteoarthritis Measures (JKOM) score, covering pain and stiffness, conditions in daily life, general activities and health conditions (subscales) were assessed for evaluation.

The results were as follows:

- The scores of subscales for the HA group were lower (better) than those for the placebo group. Meanwhile, for the "health conditions" subscale, the score of the HA group was significantly lower than that of the placebo group at all 4 time points after the initiation of administration
- JKOM score was significantly lower in the HA group than that of the placebo group at 2 and 4 months after the initiation of administration
- In patients aged 70 years or less, the difference in JKOM scores between HA and placebo was significant during early phase of administration signifying oral HA is effective in relatively young symptomatic patients

Thus, the study established the use of oral HA in managing the symptoms of OA with more prominent effects in relatively younger patients.

Source: Tashiro T, Seino S, Sato T, et al. Oral administration of polymer hyaluronic acid alleviates symptoms of knee osteoarthritis: a double-blind, placebo-controlled study over a 12-month period. *ScientificWorldJournal*. 2012;2012:167928.

SECTION 4

CONFERENCE UPDATE

2019 OARSI World Congress on Osteoarthritis: Promoting Clinical and Basic Research in Osteoarthritis

May 2-5 2019, Sheraton centre, Toronto

Role of biomechanical factors in clinical versus structural progression of knee OA

Hubley-Kozey CL.

Biochemical responses, activated by bio-mechanical factors, are associated with changes in the homeostatic balance of articular cartilage synthesis and degradation associated with OA. Earlier, cartilage degradation was the characteristic feature of OA, but gradually its effects on other structures such as muscles, ligaments, synovium and nerves came into light. Pain is the most common symptom associated

with OA. Previous studies have related biochemical responses to biomechanical loading for cartilage damage, inflammation and pain. In humans, gait studies were important in understanding knee joint-level loading in knee OA. In recent years, various studies examined muscle activation patterns including the contribution of muscles when modelling joint contact loads associated with OA processes.

- It has been shown that differences in joint movement and muscle activation patterns have been associated with the level of structural severity. It has been proven that specific pattern features are associated with increased risk of structural progression which can be defined using radiography and magnetic resonance imaging (MRI)
- Although there are less studies available which focus on biomechanical and muscle activation patterns associated with clinical severity and risk of clinical progression, there are some gait studies which state that features associated with the magnitude of joint movements are related to structural processes, whereas muscle function features and

patterns of loading are linked with clinical outcomes such as joint replacement surgery

- Aerobic exercise, particularly increasing walking frequency is recommended for OA management in terms of pain relief, improved general health and response of healthy cartilage to physical activity and exercise. This treatment is accepted world wide as non-pharmacological, non-surgical therapy for knee OA.

Therefore, it has been shown that various biomechanical targets are present for structural versus clinical OA processes. These should be taken in mind while making person-specific interventions.

Factors associated with obesity-induced changes in osteoarthritis progression

Rosen C.J.

Osteoarthritis is a degenerative disease characterized by cartilage and synovium inflammation. It is a major cause of pain and disability. Various local and systemic factors have been associated with the progression of this disease.

A study has been done to establish a relationship between obesity and OA. It included data from previous studies done. It was shown that obesity or altered metabolism affects OA and its progression. Various mechanisms were accounted for this association, such as:

- Loading-induced cartilage changes
- Inflammation due to obesity which targets cartilage in non-cell autonomous manner

- Growth and differentiation factors from infrapatellar fat pad associated with obesity
- Lipotoxicity induced metabolic syndrome
- Bone marrow lesions with increased marrow adipocyte secretion with paracrine effects on cartilage
- Cell autonomous changes in the metabolic program of the chondrocyte.

Therefore, it has been shown that various factors are associated with obesity induced changes in OA progression, thus highlighting the need of new therapeutic strategies targeting these pathogenic factors.

SECTION 5

GLOBAL NEWS

Anti-inflammatory effect of curcumin in osteoarthritis

Osteoarthritis, one of the common forms of joint inflammation, mainly affects large joints causing joint pain, swelling, stiffness and functional impairment associated with activities. Matrix metalloproteinase (MMP), a zinc-dependent protease plays a pivotal role in extracellular decomposition processes and has extracellular matrix (ECM) in pathologies such as arthritis. MMP3, a joint modulator of ECM is involved in disease morphogenesis, wound healing, tissue repair, and remodeling. It is a key characteristic of OA pathogenesis and is evidently present in osteoarthritic synovial cells and synovial tissue. With the increasing progression of OA,

Curcumin reduces cell viability, inhibits cell proliferation, increases cell apoptosis and hence, alleviates inflammation of OA by inhibiting the expression of MMP3

the goal of therapy aims at relieving symptoms and associated inflammation. Steroids and non steroidal anti-inflammatory drugs (NSAIDs) are primarily used, but due to their limited

efficacy and severe side effects such as gastrointestinal bleeding, hypertension, etc these are not used for longer duration. Curcumin, characterized by its high curative effects and minimal side effects, is an alternative therapy with anti-inflammatory properties.

In lieu of this, to evaluate the effects of curcumin on regulating MMP3 in synovial tissues of OA, a study was done on 30 osteoarthritic patients and 15 healthy controls. Microarray analysis done to screen the differential expressed genes (DEG) in synovial cells of OA included GSE1919 and GSE55235. On comparing them, it was seen that expression of MMP3 was more in osteoarthritic synovial cells. The western blot results also showed that the average expression of MMP3 in synovial cells of OA was 132% higher than that of the healthy group.

Western blot results further showed that the expression of MMP3 was 44% lower in the untreated groups compared with the curcumin group (40 micromol/L), and the expressions of FN1 and collagen III (regulators of OA) were increased by 112% and 84%, respectively, which indicated that curcumin inhibited MMP3 expression and decreased OA synovial cell activity. Flow cytometry showed that the apoptotic rate in the curcumin group increased by 85.1% compared with the untreated group. To conclude, curcumin inhibits the expression of MMP3 and promotes the cell apoptosis of OA by inhibiting MMP3, which further reduces the inflammation of OA.

Source: Zeng JJ, Wang HD, Shen ZW, Yao XD, Wu CJ, Pan T. Curcumin Inhibits Proliferation of Synovial Cells by Downregulating Expression of Matrix Metalloproteinase-3 in Osteoarthritis. *Orthop Surg*. 2019;11(1):117-125.

SECTION 6

X - RAY INTERPRETATION

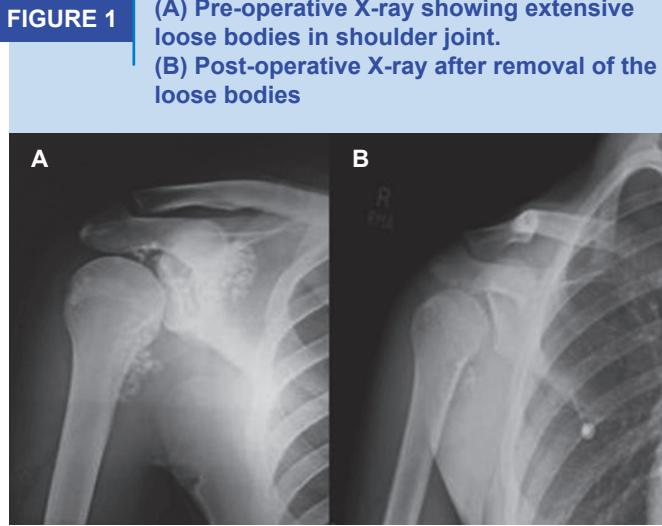
Arthroscopy

Synovial chondromatosis is a benign mono-articular arthropathy affecting synovial joints. It mostly affects knee joint, followed by hip, elbow and wrist and rarely involves shoulder joint. Pain and difficulty in movement are the symptoms usually presented. Arthrotomy, removal of chondromatoid loose bodies and synovectomy are the available treatment options. Owing to the better post operative rehabilitation and faster recovery, arthroscopic removal of the chondromatoid loose bodies is a treatment of choice.

A 20-year-old gentleman presented to the clinic with history of pain in right shoulder for 2 years and decreased range of motion. There was no history of trauma or fever. On examination he was a young gentleman with average height and built with no obvious deformity of the shoulder joint, range of motion was normal although extremes of movements at right shoulder were painful.

- Plain radiographs that included antero-posterior and scapular Y-views showed radio opaque densities in right gleno-humeral cavity, sub acromial space and medial aspect of proximal humerus (Figure 1A)
- His MRI showed presence of multiple chondromatoid bodies
- Provisional diagnosis of synovial chondromatosis was made
- Arthroscopic removal of loose bodies was planned

FIGURE 1



- Arthroscopy was done and it revealed extensive synovitis and multiple loose chondromatoid bodies. All loose bodies were removed including those which were attached to synovium, visible or palpable
- Post-operative X-rays showed clearance of the loose bodies (Figure 1B).

Source: Wahab H, Hasan O, Habib A, Baloch N. Arthroscopic removal of loose bodies in synovial chondromatosis of shoulder joint, unusual location of rare disease: A case report and literature review. *Ann Med Surg (Lond)*. 2018;37:25-29.

Arthroplasty

Osteopetrosis is an inherited disease characterized by osteosclerosis, obliteration of the medullary cavity, calcified cartilage and brittle bone due to impaired osteoclast function. OA is usually seen in patients with osteopetrosis. Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are recommended for osteoarthritic patients with osteopetrosis.

A 59-year-old female with osteopetrosis presented with a history of left hip pain and bilateral knee pain, right greater than left, with gradual activity limitation for the past 13 years. No history of fracture was reported.

- On examination, patient revealed a painful left hip and a painful right knee with limited movement
- X ray of the pelvic region showed endobones, and X-ray of spine showed "rugger jersey spine" (Figure 2), along with

severe OA in the left hip with significant acetabular erosion, proximal migration of the femoral head and reduced joint space (Figure 2). X-rays of the right knee showed similar osteoarthritic changes (Figure 2)

- THA and TKA were advised for the treatment
- A careful planning and preparation was done preoperatively and consent was taken for THA in the left hip and TKA in the right knee. Total left hip arthroplasty was performed in first instance. The THA operation was performed through a posterolateral approach (Figure 3)
- Six months later, TKA of the right knee was done. At 15-months follow-up, the components were in good position (Figure 4), and the patient could walk freely and perform activities of daily living with no pain.

FIGURE 2 Pre-operative radiographs of the spine, pelvic region and knee

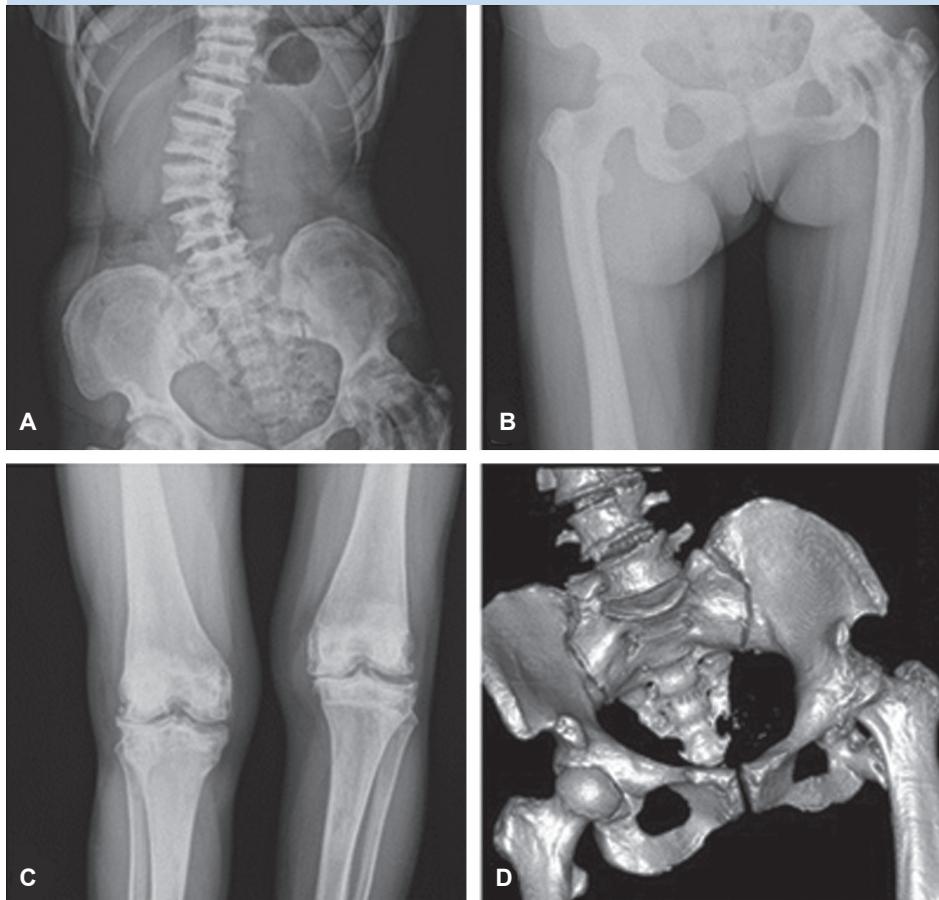


FIGURE 3 Post-operative radiograph of the left hip

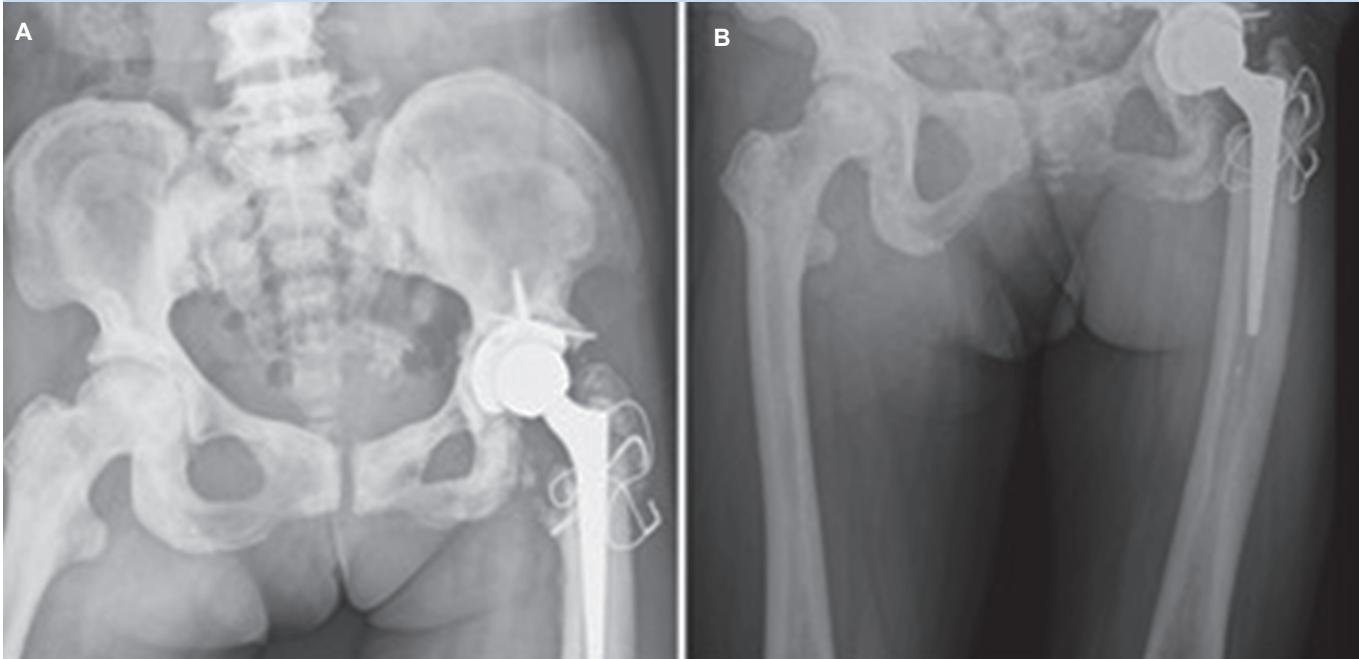
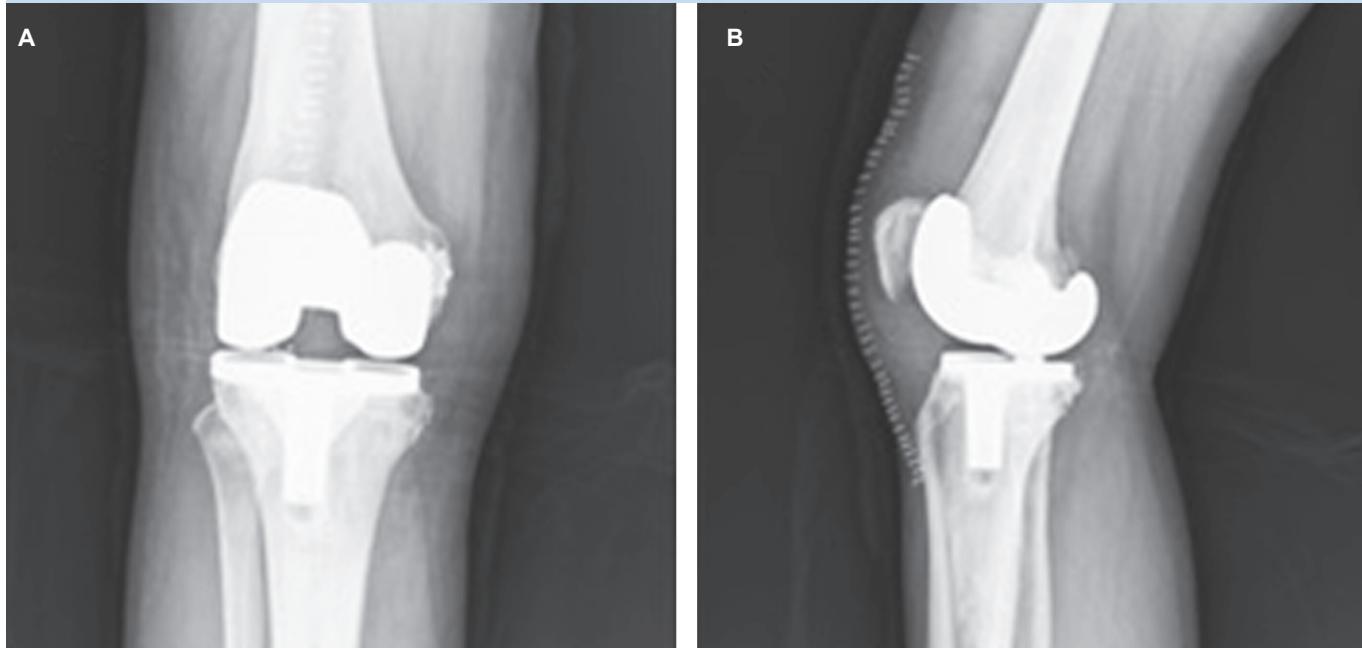


FIGURE 4 Post-operative radiograph of the right knee



Source: Xie L, Ding F, Jiao J, Kan W, Wang J. Total Hip and Knee arthroplasty in a patient with osteopetrosis: a case report and review of the literature. *BMC Musculoskelet Disord*. 2015;16:259.

Trauma

Diaphyseal tibial fractures are associated with ligament injuries in the ankle. Possessing a potential for instability and negligence, they are associated with complications such as the development of secondary OA and unfavorable functional performance when undiagnosed and untreated.

A 28-year-old male came with open fracture of right leg due to motorcycle accident. Cleaning, wound lavage, debridement of tissue lesions, and transarticular external fixation of the leg bones at the ankle joint was done to provide local damage control. X-ray showed open diaphyseal fracture of the leg classified as Gustilo IIIA (Figure 5).

On improvement of the soft-tissue envelope of the right leg, internal fixation was performed with a locked intramedullary nail for the tibial fracture (Figure 6). Open reduction and internal fixation of the ankle fracture-dislocation with plate and screws in the fibula was done. Final radiography showed a joint incongruity of the fibula with a multifragmentary fracture line on the first postoperative day. Axial computed tomography of the ankle confirmed the existence of a previous tibiofibular subluxation (Figure 7).

FIGURE 5

Open diaphyseal fracture of the right leg



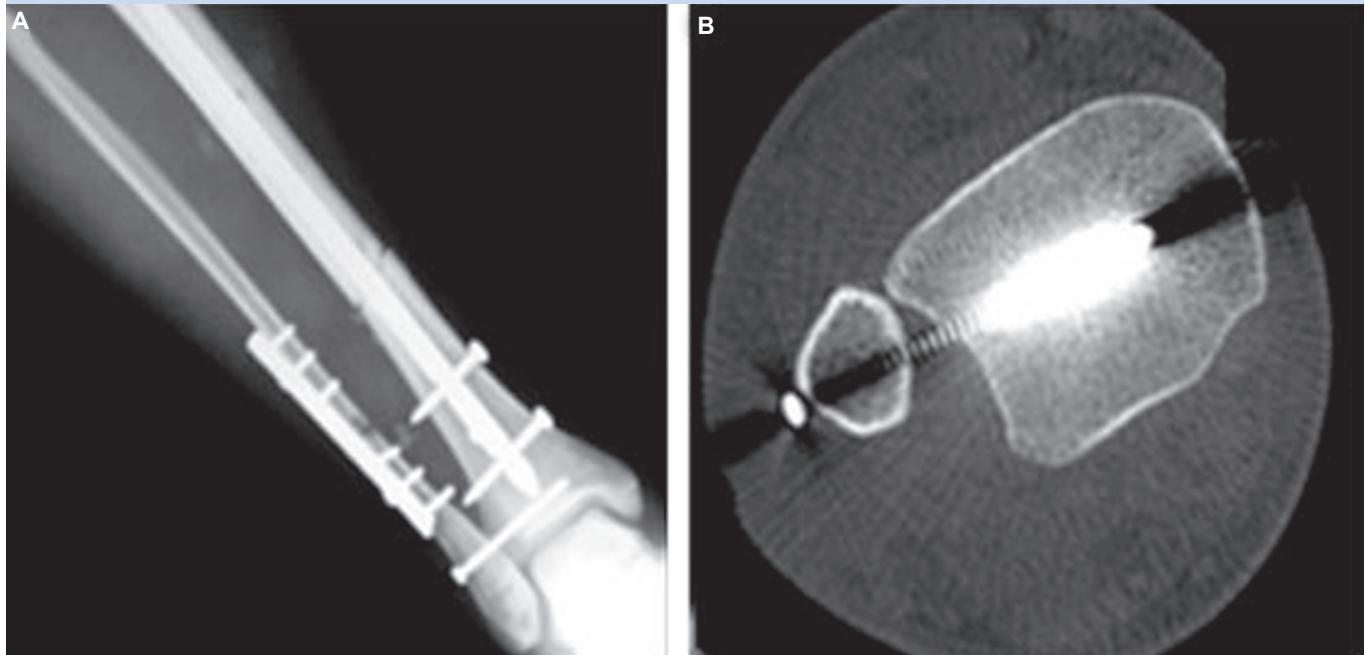
FIGURE 6

Radiograph showing insertion of the intramedullary nail, (A) Anteroposterior (AP) and (B) lateral view



FIGURE 7

(A) Radiography after open reduction and internal fixation of the fibula on AP view. (B) Axial plane CT scan showing the incongruity of the distal tibiofibular joint and its subluxation.



Source: Zamboni C, Foni NO, Souza RC, et al. Tibial shaft fracture and ankle injury – Case report. *Rev Bras Ortop*. 2016;51(5):597–600.

CONFERENCE CALENDAR



**American Association for Hand Surgery
Annual Meeting 2020 (AAHS 2020)**

January 8-11, 2020 | Florida, United States

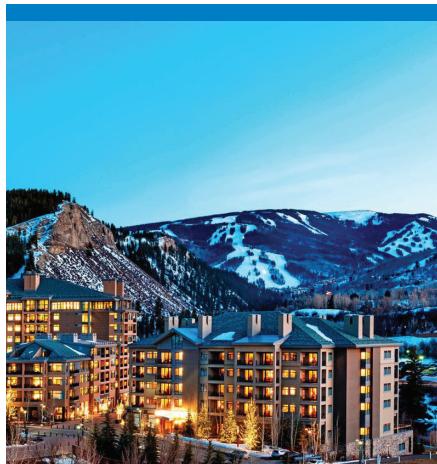
URI- <https://meeting.handsurgery.org/>



**Swedish Orthopaedic Trauma Association
Annual Meeting 2020**

January 9-10, 2020 | Stockholm, Sweden

URI- <http://www.sots.nu/>



**12th Annual ICJR Winter Hip and Knee
Course 2020**

January 16-19, 2020 | Vail, United States

URI- <https://icjr.net/meeting/2020-12th-annual-winter-hip-knee-course>

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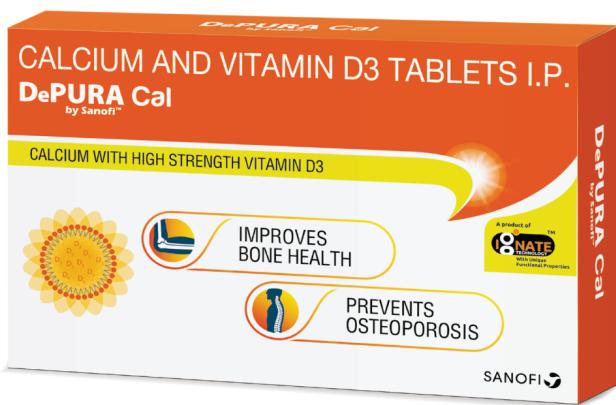
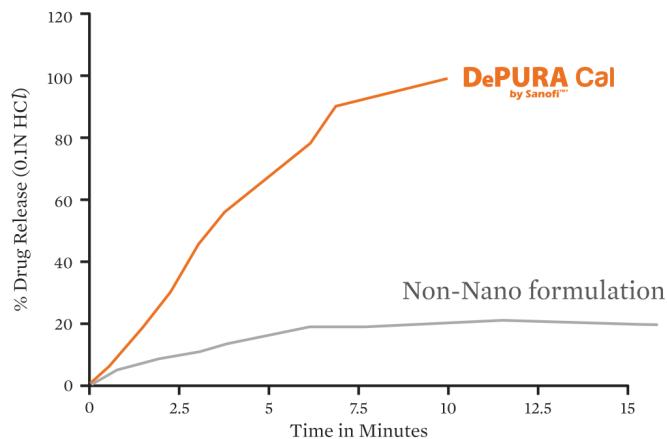
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