Ankle Osteoarthritis*

Osteoartrite do tornozelo

Alexandre Leme Godoy-Santos[1,2] Lucas Furtado Fonseca[3] Cesar de Cesar Netto[4] Vincenzo Giordano[5] Victor Valderrabano[6] Stefan Rammelt[7]

[1] Laboratório Prof Manlio Mario Marco Napoli, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil
[2] Locomotor Apparatus Program, Hospital Israelita Albert Einstein, São Paulo, SP, Brazil
[3] Department of Orthopedics, Universidade Federal de São Paulo, São Paulo, SP, Brazil
[4] Department of Orthopedics and Rehabilitation, University of Iowa, Iowa City, IA, United States
[5] Prof Nova Monteiro Orthopedics and Traumatology Service, Hospital Municipal Miguel Couto, Rio de Janeiro, RJ, Brazil
[6] Swiss Ortho Center, University of Basel, Schmerzklinik Basel, Basel, Switzerland
[7] UniversitätsCentrum für Orthopädie und Unfallchirurgie, Universitätsklinikum Carl Gustav Carus, Dresden, Germany

Address for correspondence Alexandre Leme Godoy-Santos, MD, PhD, Rua Dr. Ovídio Pires de Campos, 333–Cerqueira Cesar, São Paulo, SP, Brasil, CEP: 04503-010 (e-mail: alexandrelemegodoy@gmail.com.br).

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Abstract

Osteoarthritis (OA) is characterized by a chronic, progressive and irreversible degradation of the joint surface associated with joint inflammation. The main etiology of ankle OA is post-traumatic and its prevalence is higher among young and obese people. Despite advances in the treatment of fractures around the ankle, the overall risk of developing post-traumatic ankle OA after 20 years is almost 40%, especially in Weber type B and C bimalleolar fractures and in fractures involving the posterior tibial border. In talus fractures, this prevalence approaches 100%, depending on the severity of the lesion and the time of follow-up. In this context, the current understanding of the molecular signaling pathways involved in senescence and chondrocyte apoptosis is fundamental. The treatment of ankle OA is staged and guided by the classification systems and local and patient conditions. The main problems are the limited ability to regenerate articular cartilage, low blood supply, and a shortage of progenitor stem cells.

The present update summarizes recent scientific evidence of post-traumatic ankle OA with a major focus on changes of the synovia, cartilage and synovial fluid; as well as the epidemiology, pathophysiology, clinical implications, treatment options and potential targets for therapeutic agents.

Keywords
- osteoarthritis
- ankle
- cartilage
- synovial fluid
- therapeutics

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Resumo

A osteoartrite (OA) é caracterizada por uma degradação crônica, progressiva e irreversível da superfície articular, associada a inflamação articular. A principal etiologia da OA do tornozelo é pós-traumática e sua prevalência é maior entre os jovens e obesos. Apesar dos avanços no tratamento das fraturas ao redor do tornozelo, o risco geral de desenvolver OA pós-traumática do tornozelo após 20 anos do trauma é de quase 40%; especialmente nas fraturas bimaleolares de Weber tipo B e C e fraturas envolvendo a borda tibial posterior. Nas fraturas do tálus, essa prevalência se aproxima de 100%, dependendo da gravidade da lesão e do tempo de seguimento. Nesse cenário, é fundamental a compreensão atual das vias de sinalização moleculares envolvidas na senescência e apoptose dos condrócitos. O tratamento da OA do tornozelo é estagiado e guiado pelos sistemas de classificação, condições locais e do paciente. Os principais problemas são a limitada capacidade de regeneração da cartilagem articular, o baixo suprimento de sangue e a escassez de células-tronco progenitoras.

A presente atualização resume evidências científicas básicas recentes da OA pós-traumática do tornozelo, com foco principal nas alterações metabólicas da sinóvia, da cartilagem e do líquido sinovial. Epidemiologia, fisiopatologia, implicações clínicas, e opções de tratamento são também discutidas.

Palavras-chave

- osteoartrite
- artrose
- tornozelo
- cartilagem
- líquido sinovial
- terapêutica

Introduction

Osteoarthritis (OA) is a syndrome characterized by articular cartilage degeneration, subchondral bone changes, intra-articular inflammation and periarticular bone growth, often associated with typical symptoms of stiffness, swelling and pain in the affected joint.[1–4] An effective cure for this syndrome is still far away, be it through prevention methods, delaying its progression or proposed symptomatic treatments.[1–3,5,6]

Lower limbs OA affects ~ 15% of the world population, and it is a major cause of disability, since global estimates suggest that 250 million people are currently affected; in the United States, ~ 60 billion dollars/year are spent on its direct treatment.[1,7,8] Tibiotarsal joint OA is present in 1 to 4% of patients seeking orthopedic care due to lower limbs OA; the average age of patients at the final stage of the condition is 55.7 years. The socioeconomic impact of the disease increased along with its 300% prevalence elevation between the 1970s and the 2000s.[9]

In contrast to OA in other lower limb joints, such as the hip and the knee, which have primary and nontraumatic origin in 58% and 67% of the cases, respectively, this etiology represents only 9% of the tibiotarsal OA cases. Other secondary causes, including rheumatoid arthritis, hemochromatosis, hemophilia or osteonecrosis, are present in 13% of the cases; post-traumatic origin is the main cause, representing ~ 78% of etiologies, due to ankle fractures, ligament injuries, distal tibial fractures, tibial shaft fractures, talus fractures and combined fractures of the ankle and foot.[8–10]

Pathophysiology of post-traumatic ankle osteoarthritis

The ankle is a high congruence and stability joint, receiving high contact forces along a very thin layer of articular cartilage. This chondral structure has unique features, including more crosslinked glycosaminoglycans and fewer collagenase and interleukin (IL)-1 receptors (IL-1R) than other types of joint cartilage, which provides high rigidity and tensile strength.[11,12] As such, a change in joint congruence must occur for post-traumatic ankle osteoarthritis (OAPTT) to develop, leading to increased shear forces and accelerated degeneration.

The total area of the tibiotarsal joint is 350 mm^2, which is subjected to ~ 500 N of axial force; for comparison, the hip and knee, with joint areas of 1,100 mm^2 and 1,120 mm^2, respectively, are subjected to the same amount of force.[13–15] Thus, the pressure on the ankle joint cartilage can be up to three times greater than in other lower limb joints. The tibiotarsal cartilage thickness ranges from 1.0 to 1.62 mm, being thinner compared to the hip (1.35 to 2.0 mm) and the knee (1.69 to 2.55 mm).[16]

An acute ankle injury initiates a sequence of events in the joint milieu that can potentially lead to progressive joint surface damage in addition to direct injury to chondrocytes at the time of trauma. An increase in proinflammatory cytokines, with proteoglycan and collagen remodeling dysregulation, may play an important role in the pathogenesis of post-traumatic OA.[17–19] This can be explained by the articular cartilage limited recovery ability from a direct injury; moreover, an amplified inflammatory response of the synovial tissue is a key factor in the development of OAPTT.[20]

Recent studies have focused separately on different tissues, that is, cartilage, synovial tissue and synovial fluid. Researchers led by Adams demonstrated acute changes in the synovial fluid after an intra-articular ankle fracture. Elevation of proinflammatory cytokines, such as IL-6, IL-8, matrix metalloproteinase (MMP)-1, MMP-2, MMP-3, MMP-9 and MMP-10 can be seen within hours after a trauma. These elevations are sustained for the subacute period; in addition, an increase in other cytokines (IL-1Ra, IL-6, IL-8, IL-10, IL-15

and monocyte chemoattractant protein [MCP]-1) are observed 6 months after the injury.[21–24]

Clinical diagnosis, classification systems and supplementary investigation

In this scenario, pain is the dominant symptom and constitutes the main factor in the therapeutic decision-making process.[1] The most common clinical presentation is joint line pain associated or not with swelling (joint effusion), limited joint range of motion, and reduced locomotor function both in work-related and leisure activities.[25] Other associated clinical changes are leg muscle hypotrophy and gait pattern alterations, mainly in kinematics and kinetics.[26–29] The initial imaging investigation is performed with radiographs under load that can show different degrees of decreased joint space, formation of osteophytes, sclerosis and subchondral cysts.

The most used classification systems are the following: Kellgren-Lawrence Arthritis Grading Scale, Takakura Classification System, Morrey and Wiedeman Classification, and Classification of Osteoarthritic Changes in the Ankle (van Dijk) (►**Box 1**)[30,31]

Claessen et al evaluated the reliability of the (1) van Dijk, (2) Kellgren and (3) Takakura classification systems for posttraumatic ankle osteoarthritis and found a low grade of interobserver agreement.[31]

The most appropriate diagnostic modality for early OA detection in younger patients is magnetic resonance imaging (MRI). New techniques, such as cartilage mapping, are capable of detecting early changes in cartilaginous microstructure, extracellular matrix composition and chondrocyte biomechanics. T1ρ mapping is an important modality for assessing proteoglycan content,[32] while collagen organization is appreciated in T2 relaxation times.[33] T2 mapping has reduced sensitivity to assess deep cartilage layers, since their highly organized structural properties result in extremely short T2 relaxation times. As such, Ultrashort Echo Time (UTE) - T2 is more sensitive for accurately determining collagen integrity and cartilage degeneration.[34–36]

Single photon emission computed tomography/computed tomography (SPECT-CT) has been used in OAPTT patients to assess the extension of degenerative changes and their biological activities.[37] This imaging modality combines bone scan and immunoassay data with CT and demonstrated significantly greater inter- and intraobserver reliability compared to isolated CT or CT with bone scan.[38] In addition, SPECT-CT allows the accurate checking of mechanical misalignment effects on the cartilage. Ankles with varus deformities showed significantly higher radioisotope uptake in the medial joint compartment compared to the lateral compartment. In contrast, valgus ankles showed significantly higher uptake in lateral areas.[39,40] Computed tomography under load is an innovation in the ankle and foot field and it has shown great accuracy for diagnosis, planning and post-treatment control of ankle osteoarthritis.[41]

Box 1 Original classification systems for ankle osteoarthritis according to the Kellgren-Lawrence Arthritis Grading Scale, the Takakura classification system, the Morrey and Wiedeman classification and the Classification of osteoarthritic changes in the ankle (van Dijk)

The Kellgren-Lawrence Arthritis Grading Scale
0 - no detectable osteoarthritis
1 - doubtful narrowing of the joint space, possible osteophyte
2 - defined osteophytes, definitive narrowing of the joint space
3 - multiple osteophytes, joint space narrowing, some sclerosis
3 - large osteophytes, marked joint space narrowing, severe sclerosis.
Takakura classification system
I - early sclerosis and osteophytes formation, no joint narrowing.
II - medial joint space narrowing, no subchondral bone contact.
IIIA - medial joint space obliteration, subchondral bone contact.
IIIB - articular space obliteration over the talar domus, subchondral bone contact.
IV - joint space obliteration with complete bone contact.
Morrey and Wiedeman classification
0 - normal ankle.
1 - small osteophytes and minimal joint narrowing.
2 - moderate osteophytes and moderate joint narrowing.
3 - significant joint narrowing with joint deformation or fusion.
Classification of osteoarthritic changes in the ankle (van Dijk)
0 - normal joint or subcentral sclerosis.
I - osteophytes with no joint space narrowing.
II - joint space narrowing with or without osteophytes.
III - (sub)total joint disappearance or joint space deformation.

Biomarkers

Biomarkers are released in different body fluids after an acute fracture and can be quantified by gene expression analysis.[42,43] As OA is an inflammatory process, inflammation biomarkers can be the first signs of OAPTT. Biomarkers can be measured in blood, urine and synovial fluid. Although tumor necrosis factor alpha (TNF-α), IL-1 and some MMPs have been studied, the best marker is not yet established[44] Collagen II precursors and metabolites are more specific markers of chondrocyte metabolism and may indicate necrosis or apoptosis of such cells.[45] However, a biomarker

systematization to provide prognostic information for monitoring the clinical response to OAPTT treatments is still lacking.

Staged Treatment

The therapeutic decision must be based on the following factors:

- Intensity of joint degeneration
- Osteoarthritis etiology
- Affected joint area – asymmetric OA
- Bone quality
- Lower limb alignment
- Joint stability
- Medical history
- Condition of the patient (total arthroplasty x ankle arthrodesis)
- Experience of the surgeon

In addition, it must consider the four proposed treatment stages:

1. Nonsurgical treatment
2. Joint-sparing surgery
3. Total ankle arthroplasty
4. Ankle arthrodesis

Stage I. Nonsurgical treatment - It represents the therapeutic option for patients with initial osteoarthritis and mild, nondaily pain, with little functional limitation, good bone quality, adequate lower limb alignment, stable joint and any age group. Its goals are to improve symptoms and maintain the range of motion for a potential future surgical treatment.[10]

Orthotics and insoles

Orthotics and insoles reposition the joint, align the mechanical axis of the lower limb and correct minor changes in physiological alignment, resulting in symptomatic improvement. There is no evidence in the literature regarding clinical outcomes at long-term follow-up times.[46–48]

Physical Therapy

The literature on knee osteoarthritis rehabilitation presents good level I and II studies. However, randomized clinical studies are still required to improve evidence regarding the real role of physical therapy for articular degeneration in other joints, including the hip, hand, foot, ankle, shoulder and spine.[49]

In mild and moderate OAPTT, physical therapy helps preserving the range of motion because it increases joint stability through muscle strengthening; this is a useful feature even for future treatments through total ankle arthroplasty.[9]

Medication

Despite the high prevalence of OAPTT, there is little clinical evidence on the impact of drug treatment, since the existing literature is based on studies with small sample sizes and methodological limitations. Guidelines for drug use in foot and ankle conditions are generally extrapolated from studies in other lower limb joints. Low-dose acetaminophen and topical nonsteroid anti-inflammatory drugs (NSAIDs) are considered adjuvant for pain treatment. In case of failure, oral NSAIDs or cyclooxygenase (COX)-2 inhibitors can be added to this first line of therapy.[50]

Intra-articular injections

Evidence on steroid injections for ankle osteoarthritis is limited to four case series, totaling 298 people, with positive symptomatic responses to triamcinolone and betamethasone consisting in partial reductions of average visual analog scale (VAS) values for pain in 35% of patients.[51]

Nineteen studies present evidence on viscosupplementation with hyaluronic acid (HA), including 11 case series, totaling $\sim$ 400 patients. Positive symptomatic responses based on pain and mobility scores, VAS and SF-36 were observed in 68% of the patients. Most studies have found significant benefits from 6 to 18 months.[46–48]

Evidence on platelet-rich plasma (PRP) is based on case series totaling 45 subjects with unsatisfactory or partial responses at VAS for pain, Japanese Society for Surgery of the Foot (JSSF) ankle/hindfoot scale and the Self-Administered Foot Evaluation Questionnaire (SAFE-Q).[33–35]

Stage II. Joint-sparing surgery - This is a therapeutic option for patients with moderate osteoarthritis, significant, daily pain, small to moderate functional limitation, posttraumatic or primary etiology, good bone quality and asymmetric alignment of the lower limbs associated or not with joint instability; it is mostly indicated for young people and patients with no systemic comorbidities.

Its goals are to reestablish joint biomechanics, alignment and stability, in addition to slow down joint degeneration evolution at the most affected compartment, allowing postponement of more invasive procedures for 5 to 10 years.[10]

Articular debridement and distraction

Nonsparing procedures may not be the treatment of choice, especially in younger patients with moderate OAPTT, due to the potential for late complications and the high rates of reoperation, prosthesis failures and/or the development of secondary OA in adjacent joints.

Such patients may be submitted to open or arthroscopic debridement to relief symptoms and provide a better joint assessment[52]

Joint distraction is a viable treatment option for selected patients with OAPTT and preserved hindfoot mobility[53] The current literature does not demonstrate superior outcomes for these modalities in comparison to other joint sparing procedures.

Herrera-Perez et al demonstrated some different outcomes in a prospective, randomized study comparing isolated joint debridement and joint debridement associated with distraction. These authors observed that patients undergoing isolated debridement had a higher level of pain at the 3-year follow-up compared with the group submitted to the combined

procedure. Both treatment options can help delay the need for nonsparing procedures (arthrodesis or arthroplasty).[54,55]

Osteotomies around the ankle

The role of supramalleolar osteotomies is based on force rebalancing in the ankle joint; these procedures aim to realign the hindfoot, transfer the joint support axis to the less degenerate compartment and normalize the direction of the sural triceps force vector to delay ankle joint arthritis progression.[56–58]

The principles of supramalleolar osteotomy are the following:

1. To locate the deformity apex: the deformity vertex is often close to the joint surface or positioned within the joint; in this situation, correction through the apex may not be possible. Corrections made outside the proper level result in distal fragment translation. As such,
   - wedge osteotomies proximal to the apex lead to ankle joint medialization when valgus is corrected
   - wedge osteotomies proximal to the apex lead to ankle lateralization during varus correction

   In these cases, lateral overload on ankles with valgus OA and medial overload on the ankles with varus OA will be sustained, and additional compensatory translation is critical:
   - lateral translation in valgus ankles
   - medial translation in varus ankles
2. To recognize the joint pattern: congruent or incongruous type
3. To perform additional procedures if required
   - sagittal plane correction
   - distal fibula length and orientation adjustment
   - soft tissue balancing

The authors observed encouraging medium-term outcomes after supramalleolar osteotomies in patients with intermediate-staged OAPTT, with significant pain relief and functional hindfoot improvement according to the American Orthopaedic Foot and Ankle Society (AOFAS) score, often requiring additional procedures.[56–58]

Stage III. Total ankle arthroplasty - This is a therapeutic option to address severe osteoarthritis associated with high-intensity daily pain and high functional limitation. It presents better outcomes in young patients with post-traumatic conditions, adequate bone stock, proper lower limbs alignment or mild asymmetry and joint stability who do not present serious systemic comorbidities. This procedure can be indicated for patients with severe OA but not the previously described features; however, in these cases, complication (including infection, dehiscence, residual pain and reduced range of motion) and reoperation rates are high.[59–61]

Absolute contraindications to total ankle arthroplasty (ATT) include:

- acute or chronic infections, with or without osteomyelitis
- total avascular necrosis of the talus body

Relative contraindications include:

- severe osteoporosis
- bad bone quality
- diabetes mellitus
- smoking
- overweight/obesity

Patients already submitted to ankle prosthesis procedures and presenting with component failure or wear may require a review arthroplasty; however, this is a technically demanding surgery. Painful pseudoarthrosis or vicious arthrodesis consolidation are another specific indication for total ankle replacement.[59]

Modern implants are three-component systems: a talar component, a tibial base component and a modular tibial joint surface. Recent advances related to implant design provide less bone resection, better bone-implant fixation and longer component durability. The procedure can be performed through an anterior or lateral transfibular access route.[59–61]

Total ankle arthroplasty studies show clinical and pain scores improvement in up to 64% of the cases. Total ankle arthroplasty using modern implants shows success rates of 70 to 90% in 10 years. Although age, body mass index (BMI) and preoperative deformity degree are not associated with higher failure rates, patients with hindfoot arthrodesis presented a significantly higher risk of implant failure (►**Figure 1**)[59–62]

Stage IV. Ankle arthrodesis - Arthrodesis is mainly indicated for cases of severe osteoarthritis, failure of the previous options, high functional limitation, secondary to any etiology, and in patients of any age group.

Total ankle replacement and tibiotarsal arthrodesis are the treatment modalities for end-stage ankle osteoarthritis. Formerly recognized as the gold standard, ankle arthrodesis was indicated in the vast majority of cases due to its predictable results and lower complication rates. The development of ATT modified this therapeutic decision-making algorithm, demonstrating, at least, better biomechanical and functional outcomes. The increase in movements of adjacent joints during postarthrodesis follow-up, as a form of biomechanical compensation, is not a consensus yet, and these joints may suffer medium- and long-term progressive degeneration.[63–67]

There are four main differences in the biomechanical function of arthroplasty compared to arthrodesis:

- faster walking speed
- increased forefoot joint range of motion at the sagittal plane
- increased sagittal hindfoot movement
- increased ankle plantar flexion

For mild and moderate deformities, the arthroscopic or mini-open route are safe options; for severe deformities, however, the anterior and lateral transfibular routes are more indicated.[68]

Consolidation rates for these techniques range from 72 to 93%, but nonunion rates in smokers are as high as 54%.[69] The most frequent complications are wound dehiscence,

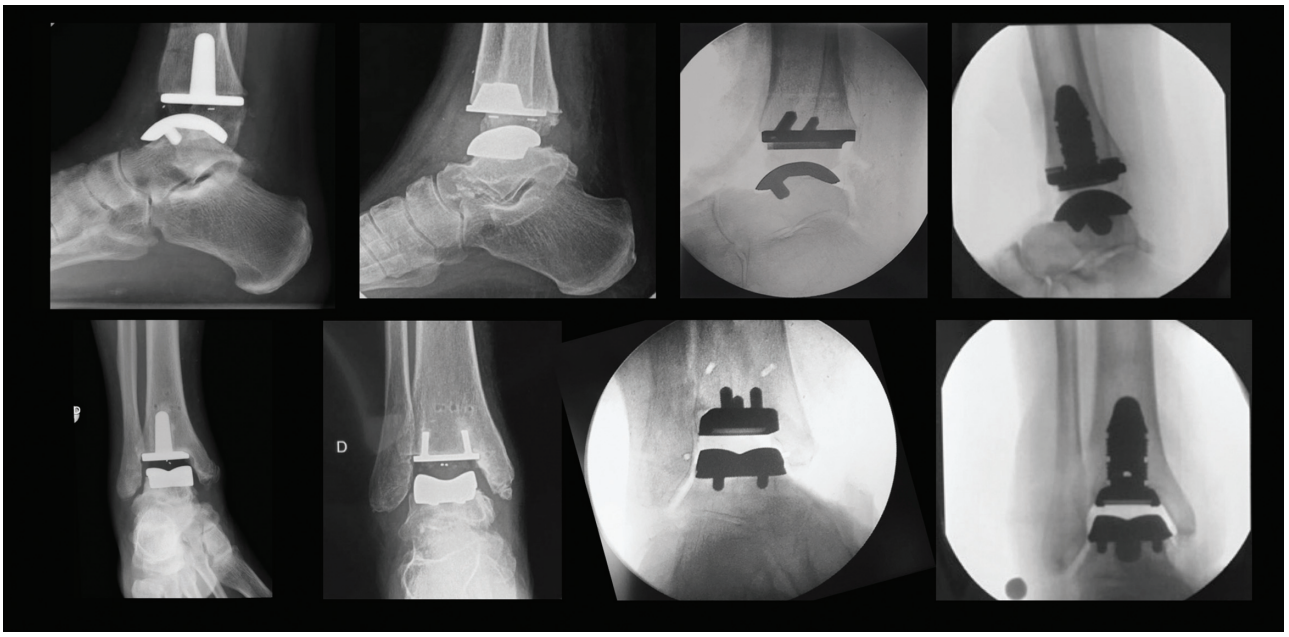

Fig. 1 Drawings of total ankle prostheses available in Brazil in lateral (upper column) and anteroposterior (lower column) views. ZENITH / Corin Group, TARIC / ImplanCast, INFINITY / Wrigth Medical, INBONE / Wrigth Medical.

superficial infection and neuroma; review procedures are required in 7 to 9% of cases, regardless of the technique used[70]

Final Considerations

Ankle OA is a different clinical situation from knee and hip OA, and it is mainly caused by traumatic injuries. The identification of molecular and cellular mechanisms involved in this condition are in focus in the literature. In the near future, the use of intra-articular and systemic medications that modulate the inflammatory joint response will probably play an important role in functional outcomes of fractures around the ankle, preventing even more dramatic results for this OA.

The most affected age group is composed by young adults; treatment is performed in stages and the therapeutic decision is multifactorial. Surgical options have well-defined principles and predictable functional outcomes. Viscosupplementation with hyaluronic acid and triamcinolone can be considered for nonsurgical treatment of early ankle OA.

Joint debridement associated or not with distraction represents a safe option for the treatment of stage II ankle OA. In final stages, total ankle arthroplasty and arthrodesis are the most appropriate procedures and must be discussed with the patient to make the best therapeutic decision.

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