

Osteoarthritis in the 21st century – a new paradigm: Osteoarthritis and Osteoarthrosis

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Many changes occurred in the last 40 years (within the transition between the 20th and the 21st century) in our understand and approach of Osteoarthrosis (OA). In the past, OA was identified as the degenerative articular disease paradigm (as well as Rheumatoid Arthritis was identified as the articular inflammatory disease paradigm), with a physiopathology almost unknown, but focused in changes in cartilage, and which was associated to a conviction of inevitability in the progression and near absence of effective therapeutic interventions.

In recent years there has been a remarkable evolution in the knowledge of the pathophysiological mechanisms that contribute to the onset and evolution of OA. This allowed us to realize that this is not a fatality, but a clinical condition that can be intervened in order to modify its evolution and change its consequences.

Thus, rather than a static, univocal diagnostic entity, OA must come to our understood as an **evolving disease**, with variable pathogenic and clinical expressions throughout its evolution, but in which only a progression of the pathogenic process of the disease, with absence or insufficiency of therapeutic intervention (pharmacological and non-pharmacological), capable of preventing or slowing down this progression, will lead to a consequent erosion of the structural and functional reserve of the joint, and the appearance of forms of evolved OA, true **joint insufficiency** (similar to any chronic insufficiency of another organ or system).

So, OA should no longer continue to be seen as a static diagnosis, an absolute "label" for all patients, but as a range of distinct clinical situations throughout its pathogenic evolution, from early to late stages of joint destruction. And understood more as a concept not of a true Disease, but of a **Syndrome** (a disorder with common clinical characteristics, and with similar forms of clinical approach, in which different causes and dif-

ferent pathophysiological mechanisms are globally expressed in several joint structures, in different ways depending on the stage of disease evolution)¹.

Throughout the progressive understanding of the pathogenic mechanisms of OA, some aspects must be considered of enormous clinical relevance, with a decisively impact on the way we understand and therapeutically manage the disease:

- the understanding of the disease not as a cartilage pathology, but as a disease of all joint structures (with joint understood as an organ), with central impact on the cartilage, but with a fundamental pathogenic role of the subchondral bone-cartilage unit (this unit - BCU²- being understood as a complex biological functional unit, interacting through cellular and molecular interactions), as well as primary importance of the synovial membrane inflammation (in a real disruption with previous concepts of an absence of synovial inflammation in OA)^{3,4};
- the identification of evident and crucial inflammatory occurrences in the onset and evolution of OA (especially in its earliest stages), evident in clinical terms (the inflammatory pattern of pain/existence of joint inflammatory signs), and imaging evidences. Here, the complementary method of choice would be MRI, as there is a lesion (bone marrow edema - BML) which, at an early stage of diagnosis (pre-radiographic), constitutes an element of identification, but also of prediction of the risk of symptoms and structural evolution, with the corresponding implications in terms of clinical approach⁵. However, joint ultrasound is currently the most efficient and accessible complementary diagnostic tool to detect early and easily these inflammatory elements in early OA - the synovial membrane presents inflammatory features in these early stages of OA, still knowing that synovial hypertrophy and a Doppler signal on ultrasound correlate with faster radiographic progression^{6,7,8}.
- the evidence of distinct OA phenotypes^{9,10} and their

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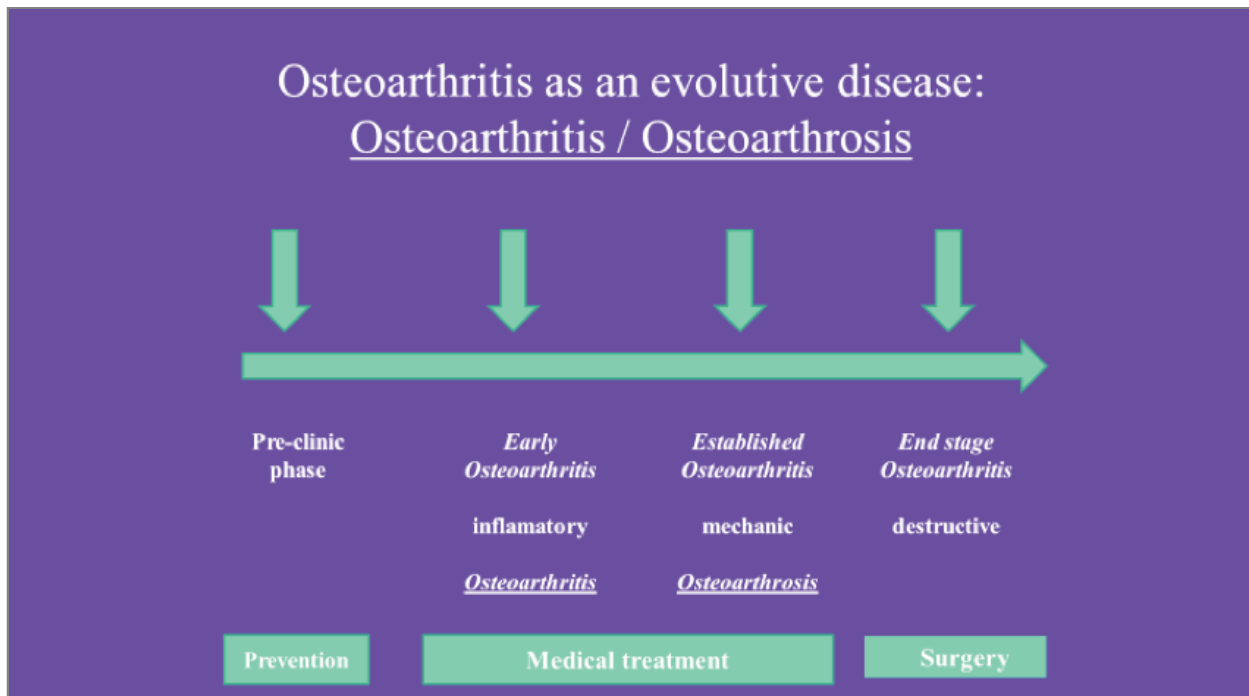


FIGURE 1. Osteoarthritis as an evolutive disease.

underlying mechanisms, allowing individualization of therapy for these patients, namely:

- * Biomechanical (increased biomechanical stress: related to overweight, joint misalignments, ligament and meniscal changes...);
- * Inflammatory (existence of more exuberant synovitis than the low-grade inflammation observed in the other phenotypes);
- * Metabolic (by the increase of pro-inflammatory adipokines associated with diabetes mellitus, metabolic syndrome, obesity, and other cardiovascular risk factors);
- * Osteoporotic (related to hypoestrogenism, which leads to increased remodelling and changes in trabecular and subchondral bone).

In summary, the main changes in the understanding of OA in recent years are:

- the perception of the disease as a continuous entity, with multiple clinical presentations throughout its pathological evolution;
- the identification of standardized clinical presentations (phenotypes), allowing more specific therapeutic approaches;
- an improved knowledge of its pathophysiology, creating the opportunity to think of specific therapeutic targets in the short and medium-term;

- the unequivocal demonstration of the importance of multiple inflammatory phenomena (UBC and synovial membrane) in the evolution and clinical presentation of OA (especially in its earliest stages), implying the corresponding need to adjust our therapeutic management.

In the heterogeneity and continuous evolution of the disease, there are two paradigms of disease presentation that must be considered:

- a) "**Inflammatory OA, true Osteoarthritis**": an early and incipient stage, in which synovial inflammation and microscopic changes at bone and cartilage level are predominant, potentially modifiable with appropriate pharmacological approaches; this is the OA that is the paradigm of the current demand for early diagnosis, with the highlight of the inflammatory aspects of the disease (true osteoarthritis), implying that our therapeutic management should be adapted to these aspects;
- b) "**Mechanical OA, true Osteoarthrosis**": classic paradigm of mechanical degenerative joint disease (true osteoarthrosis), representing more advanced stages of its evolution and a late diagnosis of evolved disease, with destructive changes of all joint structures, leading to pain and disability, difficult to fully resolve with pharmacological therapy; a "me-

chanical osteoarthritis", which in its progression often evolves to "terminal" (surgical) forms of the joint.

Thus, in this new paradigm of terminology, Osteoarthritis is not the same as Osteoarthritis¹¹, and these should be distinct clinical phenotypes to be used according to distinct clinical frameworks:

Osteoarthritis:

- inflammatory pain
- clinical identification of joint inflammatory evidence
- X-ray with discrete changes (reduced ILA)
- Ultrasound revealing synovial inflammation or joint effusion.

This diagnosis of Osteoarthritis may, in earlier stages of the disease, may pose a differential diagnosis with some forms of undifferentiated arthritis, serving as identifying elements of the former condition the pattern and location of the joints involved, the lower magnitude of joint inflammation, or the absence of systemic inflammatory biomarkers.

Osteoarthrosis:

- mechanical pain
- clinical identification of joint deformities
- X-ray showing marked changes (subchondral sclerosis and osteophytosis)
- Ecography revealing structural lesion, namely osteophytosis.

In the end, with this paradigm shift and based on these current concepts, a new clinical attitude is essential, which is to focus our intervention on the individual patient (listening to and observing the patient and characterizing his/her complaints), defining individual intervention strategies, knowing that treatment should be as early as possible, and that, as OA is a chronic disease, treatment should be daily and permanent, and that this treatment always implies several therapeutic targets, varying according to the clinical situation. Knowing that the evolution of OA is not a fatality and that adequate and timely clinical intervention can modify the natural evolution of the disease and its global impact.

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