Rapid Destructive Osteoarthritis

September 8-9, 2020

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Osteoarthritis (OA) Overview

OA has an indolent natural progression characterized by:

- Degradation and loss of the articular cartilage
- Joint space narrowing
- Changes in subchondral bone structure
- Osteophytes at the joint margins
- Variable degrees of synovitis with synovial hypertrophy
- Thickening of the joint capsule

Clinical and imaging features of end-stage OA include:

- Loss of articular cartilage
- Subchondral bone cysts
- Synovitis
- Joint deformity
- Changes in peri-articular structures
- Loss of normal joint function

OA: Osteoarthritis

Loeser F. Age-related changes in the musculoskeletal system and the development of osteoarthritis. *Clin Geriatr Med.* 2010;26(3):371–86.
Robinson WH, Lepus CM, Wang Q, et al. Low-grade inflammation as a key mediator of the pathogenesis of osteoarthritis.*Nat Rev Rheumatol.* 2016;12(10):580–92.
OARSI. Osteoarthritis as a Serious Disease. 2016. Available here.

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Rapid Destructive OA (RDOA) Is a Clinically Distinct Form of OA

OA

Characterized by pathology involving the whole joint, including cartilage degradation, bone remodeling, osteophyte formation, and synovial inflammation

RDOA

Characterized by abnormal destruction of subchondral bone and joint collapse, typically occurs within 12 months

Although RDOA has features of OA, bone loss and joint collapse are not normally present in end stage OA

RDOA*

- First described in 1957
- May be misdiagnosed as osteonecrosis, septic arthritis, and crystalline arthropathy
- Typically unilateral
- Mostly observed in the hip, also seen in shoulder and knee

*Sometimes other terms such as rapidly progressive OA type 2 are used to describe RDOA, but RDOA is the most common and widely accepted by physicians

OA: Osteoarthritis; RDOA: Rapid Destructive OA

Kolasinski SL, Neogi T, Hochberg MC, et al. American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. *Arthritis & Rheumatology*. 2020;72(2):220-233.
Flemming DJ, Gustas-French CN. Rapidly Progressive Osteoarthritis: a Review of the Clinical and Radiologic Presentation. *Curr Rheumatol Rep.* 2017;19(7):42.
Pivec R, Johnson AJ, Harwin SF, Mont MA. Differentiation, diagnosis, and treatment of osteoarthritis, osteonecrosis, and rapidly progressive osteoarthritis. *Orthopedics.* 2013;36(2):118-125.

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RDOA Is Typically Diagnosed and Identified on Radiographs

Radiographs of RDOA show evidence of bone loss and joint collapse which is not typical of end-stage OA

End Stage OA in the hip

RDOA in the hip

End Stage OA in the knee

RDOA in the knee

RDOA: Rapid Destructive Osteoarthritis

1. Data on File, Pfizer Inc.

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Emerging Literature Suggests Cases of RDOA Are Increasing with the Aging Population and the Study of Potential New Therapies

Causes of RDOA:

- Idiopathic
- As an adverse event with established therapeutics (e.g., NSAIDs, intraarticular corticosteroid injections) and investigational products (e.g., NGF inhibitors)

Factors that May Increase Risk of RDOA:

- Poor bone integrity
- Crystal-induced arthritis
- Biomechanical factors
- Certain joint conditions
  - Subchondral insufficiency fractures

RDOA: Rapid Destructive Osteoarthritis; NSAIDs: Nonsteroidal Anti-inflammatory Drugs; NGF: Nerve Growth Factor

1. Flemming DJ, Gustas-French CN. Rapidly Progressive Osteoarthritis: a Review of the Clinical and Radiologic Presentation. Curr Rheumatol Rep. 2017;19(7):42.

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In Clinical Trials, Investigational NGF Inhibitors Have Been Shown to Have an Increased Risk of Developing Pathology Consistent with RDOA Versus Comparators

Therapy	Tanezumab*[1]	Fasinumab*[2]	Fulranumab*[3]
Clinical Trial	In a Phase III clinical trial, 0.3% and 1.4% of patients treated with 2.5 and 5mg tanezumab respectively and 0.1% of patients treated with NSAIDs developed RDOA	In a Phase IIb/III clinical trial, 0.3% patients treated with 1-6mg of fasinumab and no patients treated with placebo developed RDOA	In a Phase II clinical trial, 0.8% of patients treated with 1-10mg of fulranumab developed RDOA

In the real-world setting, tracking of RDOA will be challenging without an ICD-10-CM code.

*No NGF inhibitor is approved by the FDA for any use. The safety and efficacy have not been established.
NSAID: Nonsteroidal Anti-inflammatory Drugs; NGF: Nerve Growth Factor

1. Hochberg MC, Carrino JA, Schnitzer TJ, et al. Subcutaneous Tanezumab Versus NSAID for the Treatment of Osteoarthritis: Joint Safety Events in a Randomized, Double-Blind, Active-Controlled, 80-Week, Phase-3 Study *ACR/ARHP Annual Meeting,* November 8-13, 2019.
2. Dakin P, DiMartino SJ, et al. The Efficacy, Tolerability, and Joint Safety of Fasinumab in Osteoarthritis Pain: A Phase IIb/III Double-Blind, Placebo-Controlled, Randomized Clinical Trial. *Arthritis & Rheumatology*. 2019; 71(11):1824–1834.
3. Moskowitz R, Brandt K, Lequesne M, et al. Adjudication Process for Joint Events of Interest in Fulranumab Clinical Trial Program. *Osteoarthritis Cartilage*. 2013;21(Suppl 1) :S288-S289 <abstract #564>

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In Tanezumab Studies Two Types of Rapidly Progressive OA Have Been Described

Rapidly progressive OA Type 1

Defined as a significant loss of joint space width ≥2mm (predicated on optimal joint positioning) within approximately 1 year, without gross structural failure

This describes progression of OA at a faster rate than normal and could be coded under current OA codes as the pathology is the same and therefore distinct from RDOA

Rapidly progressive OA Type 2

Defined as abnormal bone loss or destruction, including limited or total collapse of at least one subchondral surface, that is not normally present in conventional end-stage OA

This describes the same pathology as RDOA, for which a code does not exist. Therefore the request is that rapidly progressive osteoarthritis Type 2 be added as an inclusion to RDOA code

NGF: Nerve Growth Factor; OA: Osteoarthritis; RDOA: Rapid Destructive Osteoarthritis

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The Ability to Code Accurately Should Allow More Precise Healthcare Services Research and Ultimately Lead to Improved Patient Outcomes

Limit miscoding

With a code to accurately reflect a diagnosis of RDOA, there will be less risk for miscoding

Reduce underreporting

There are likely more cases than what is reported because of a lack of code

Understand etiology

The ability to code accurately would improve safety tracking and could advance the understanding of disease etiology

RDOA: Rapid Destructive Osteoarthritis

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