

Fatty Degenerative Osteonecrosis of the Jaw: Bridging Molecular Insights and Clinical Practice - Scoping Review

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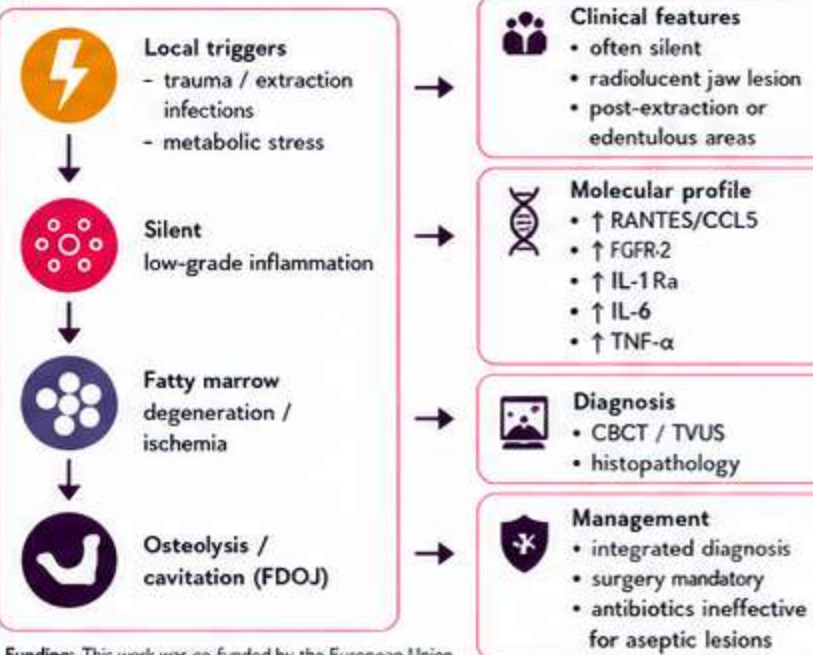
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 Type of work: Scoping review



1. GRAPHICAL ABSTRACT



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2. BACKGROUND AND OBJECTIVE

- FDOJ is a chronic, aseptic, ischemia/inflammatory condition of the jawbone.
- This review integrates molecular pathway, imaging findings, histopathology, clinical presentations, and treatment considerations to provide a comprehensive overview for diagnosis and management.

3. MATERIAL AND METHODS

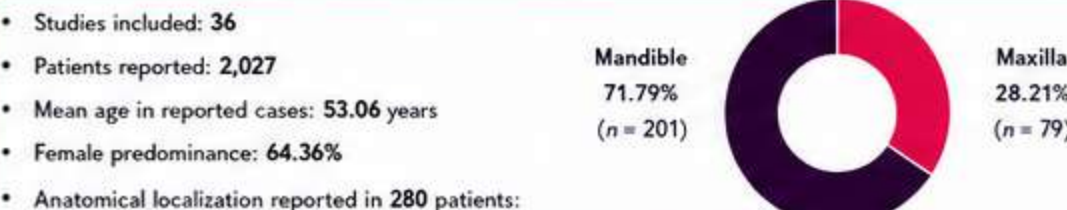
- Review type:** scoping review (method according to PRISMA-ScR guidelines)
- Database:** PubMed, Scopus, and Embase
- Search period:** from inception to July 2025
- Search terms:** fatty marrow, osteonecrosis, inflammation, jaw, bone marrow necrosis, fatty degeneration, histopathology, osteonecrosis, jawbone

4. EVIDENCE SELECTION (PRISMA-ScR SUMMARY)



Flow diagram based on PRISMA-ScR recommendations.

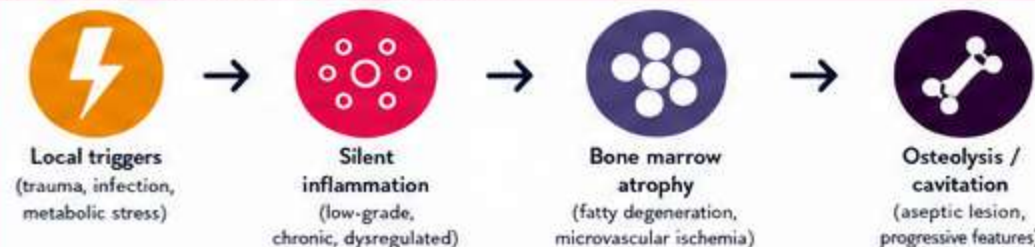
5. EVIDENCE BASE AND STUDY PROFILE



6. MOLECULAR AND HISTOPATHOLOGICAL SIGNATURE

Category	Biomarker	Observed Change	Clinical Interpretation
Molecular (Biomarker)	CC motif chemokine ligand 5 (RANTES / CCL5)	Elevated	Central chemokine in chronic inflammation inflammatory and persistent inflammatory context in the lesion milieu
	Fibroblast growth factor-2 (FGF-2)	Elevated	Reflects tissue damage, hypoxia response, angiogenesis, and fibroblastic remodeling
	Interleukin-1 receptor antagonist (IL-1Ra)	Elevated	May support controlled inflammatory activation while regulating chronic inflammation.
	Interleukin-6 (IL-6)	Reduced	Supports the low-inflammatory, clinically silent phenotype
	Tumor necrosis factor-alpha (TNF-α)	Reduced	Downward contribution to osteoclast inactivity and decreased resorption.
Histopathologic (Hallmarks)	Fatty degeneration, osteolysis, infarction, fibrosis, chronic inactive bone inflammation, necrotic adipocytes, and marrow ischemia, ultimately infarction		Characteristic microscopic features explaining the aseptic, low-grade inflammatory scenario.

9. PROPOSED PATHOGENETIC CONCEPT



Concept summary: Persistent local triggers and cytokine imbalance promote fatty degeneration and marrow ischemia, ultimately leading to osteolysis and cavitation within an inflamed clinical phenotype.

7. DIAGNOSTIC APPROACH

	Clinical suspicion	Often silent; consider history of extraction, neurologic symptoms, inflammation.
	Two-dimensional imaging	Orthopantomogram and periapical radiographs may be insufficient.
	Advanced imaging	CBCT / TVUS / intra-oral US / ultrasonography improves detection of subtle intraosseous fatty changes.
	Confirmation	Histopathology and immunohistochemical studies when clinically required.

8. CLINICAL IMPLICATIONS AND TREATMENT

- Treatment principles**
Surgical removal of necrotic bone remains the primary treatment modality; antibiotic therapy is ineffective for aseptic lesions.
- Antibiotics**
Differential diagnosis should include odontogenic cysts, traumatic bone cyst, central giant cell granuloma, fibroma, and metastatic diseases.
- Adjunctive approaches**
Adjunctive immunomodulatory strategies aimed at chemokine pathways are promising but insufficiently standardized.

10. CONCLUSIONS

Fatty degenerative osteonecrosis of the jaw is a clinically silent, aseptic osteonecrotic process with a regulated molecular profile. Integrated assessment using advanced imaging, molecular data, and histopathology is critical for accurate risk stratification and effective clinical management.

11. LIMITATIONS AND FUTURE DIRECTIONS

- Heterogeneous terminology and diagnostic criteria limit direct comparability across studies.
- Standardized imaging and reporting, targeted prospective studies validating molecular and imaging markers, histopathological confirmations, risks, and treatment protocols are needed.
- Future studies should test whether molecular markers can predict treatment associations or treatment outcomes.

12. SELECTED REFERENCES

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