I would like to make a systematic review or meta analysis regarding the risk of Medication-Related Osteonecrosis of Jaw after dental treatment between patient who has taken anti-resorptive medication and patient who has not taken such medication. Using a PICO search model. //P: Regardless of age and sex, Osteoporosis patients, excluding cancer patients //I: Monoclonal antibody (Romosozumab) //C: no history of anti-resorptive medication use //O: incidence of Medication-Related Osteonecrosis of Jaw after invasive dental procedure (including teeth extraction, periodontal surgery, implant insertion, removable prosthesis, etc)

Current research shows romosozumab has a lower MRONJ risk compared to other anti-resorptive medications but lacks comparison with non-medicated patients.

Abstract

In osteoporosis patients undergoing invasive dental procedures while on anti-resorptive treatment, the reported incidence of MRONJ varies widely. In a large procedure-based study, Penoni et al. document a 0.03% rate (2 cases in 6,742 procedures) associated with tooth extractions and prosthesis adjustments, whereas Kwack and Park report 38.2% (130 of 340 patients) after dental extractions and implantations. Tohashi et al. describe an incidence of 57.14% in a small prospective cohort, and Pichardo et al. note a 10% rate following implant procedures. Peng et al. compare medications by reporting odds ratios that range from 494.8 for pamidronate to 6.4 for romosozumab.

In these studies, dental procedures—including extractions, implant placements, periodontal surgeries, and prosthesis adjustments—are linked with MRONJ onset that ranges from at least 6 months to a median of 24 months. Risk factors include longer duration of anti-resorptive use, advanced age, multiple operated teeth, local surgical factors, and higher bone mineral density. Among anti-resorptive agents, romosozumab appears associated with a lower relative risk compared to other medications, though none of the studies directly compare outcomes with those who have not received anti-resorptive therapy.

Paper search

Using your research question "I would like to make a systematic review or meta analysis regarding the risk of Medication-Related Osteonecrosis of Jaw after dental treatment between patient who has taken anti-resorptive medication and patient who has not taken such medication. Using a PICO search model. //P: Regardless of age and sex, Osteoporosis patients, excluding cancer patients //I: Monoclonal antibody (Romosozumab) //C: no history of anti-resorptive medication use //O: incidence of Medication-Related Osteonecrosis of Jaw after invasive dental procedure (including teeth extraction, periodontal surgery, implant insertion, removable prosthesis, etc)", we searched across over 126 million academic papers from the Semantic Scholar corpus. We retrieved the 497 papers most relevant to the query.

Screening

We screened in papers that met these criteria:

- **Population Type**: Does the study focus exclusively on patients diagnosed with osteoporosis WITHOUT cancer diagnoses?
- **Intervention**: Does the study examine Romosozumab treatment specifically?
- **Control Group**: Does the study include a comparison group of patients with no history of anti-resorptive medication use?
- **Outcome Measurement**: Does the study report on MRONJ as an outcome following dental procedures?
- **Study Design**: Is the study either a randomized controlled trial, prospective/retrospective cohort study, or case-control study?
- **Dental Procedures**: Does the study include invasive dental procedures (extraction, implants, periodontal surgery, or prosthetic treatments)?
- **Documentation Quality**: Does the study provide clear documentation of both the dental procedures performed AND the MRONJ diagnosis criteria used?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Data extraction

We asked a large language model to extract each data column below from each paper. We gave the model the extraction instructions shown below for each column.

- **Study Design**:

  Identify the type of study design (e.g., retrospective cohort, prospective observational, case-control). Look in the methods section for explicit description of the study design. If the design is not clearly stated, carefully review the methodology to determine the most appropriate classification.

Possible designs include:

- Retrospective chart review
- Prospective observational study
- Retrospective cohort study
- Case-control study

If multiple design elements are present, list all that apply.

- **Participant Characteristics**:

  Extract the following participant details:

- Total number of participants
- Age range or mean age
- Gender distribution
- Specific inclusion criteria (e.g., osteoporosis patients, age 55 years)
- Specific exclusion criteria

Look in the methods section under "Participants" or "Patients" for this information. If ranges are provided, record both minimum and maximum values. For percentages, include the total number and percentage for each category.

Example format:

- Total participants: [number]
- Mean age: [value] years
- Female: [number] (%)
- Male: [number] (%)
- Inclusion criteria: [detailed list]

- **Anti-Resorptive Medication Details**:

  Extract specific information about anti-resorptive medications:

- Type of medication (e.g., bisphosphonates, Romosozumab)
- Duration of medication use
- Dosage (if reported)
- Route of administration

Locate this information in the methods or participant characteristics section. If multiple medications are mentioned, list all with their specific details. If dosage or duration is reported as a range, record the full range.

If information is partially missing, note "Not fully reported" and extract any available details.

- **Dental Procedures Performed**:

  List all invasive dental procedures conducted in the study:

- Type of procedure (e.g., tooth extraction, dental implant, periodontal surgery)
- Number of procedures performed
- Specific details about the procedures

Look in the methods and results sections for comprehensive information about dental interventions. If procedures are categorized, extract the number for each category.

Example format:

- Tooth extractions: [number] (%)
- Dental implants: [number] (%)
- Periodontal surgeries: [number] (%)

- **Medication-Related Osteonecrosis of Jaw (MRONJ) Outcomes**:

  Extract detailed information about MRONJ occurrence:

- Total number of MRONJ cases
- Incidence rate (percentage of cases)
- Timing of MRONJ development
- Specific characteristics of MRONJ cases

Locate this information primarily in the results section. If multiple MRONJ characteristics are reported, extract all available details. Calculate the incidence rate if not directly provided by dividing total MRONJ cases by total procedures or participants.

Include any statistical significance or risk factors associated with MRONJ development.

- **Risk Assessment and Predictive Factors**:

  Identify and extract:

- Risk assessment methods used
- Key predictive factors for MRONJ
- Statistical methods for risk prediction
- Performance metrics of predictive models (e.g., AUC, sensitivity, specificity)

Review methods and results sections carefully. If machine learning or statistical models were used, extract details about model type, variables considered, and performance metrics.

Example format:

- Predictive model type: [e.g., machine learning, logistic regression]
- Key risk factors: [list]
- Model performance: AUC = [value]

Results

Characteristics of Included Studies

Study	Study Design	Population Size	Follow-up Period	Procedures Studied	Full text retrieved
Penoni et al., 2023	Retrospective chart review, Retrospective cohort study	6,742 procedures in patients under osteoporosis treatment	9 years (January 2012 to January 2021)	Tooth extractions, dental implant placements, periodontal procedures, removable prostheses	Yes
Kwack and Park, 2023	Retrospective chart review	340 patients	3.5 years (January 2019 to June 2022)	Dental extraction, implantation	Yes
Pichardo et al., 2020	Retrospective chart review	180 patients with Medication-Related Osteonecrosis of the Jaw (MRONJ)	16 years (January 2003 to January 2019)	Dental implants	No

Study	Study Design	Population Size	Follow-up Period	Procedures Studied	Full text retrieved
Peng et al., 2022	Retrospective cohort study	18,421 MRONJ reports	17.75 years (January 2004 to September 2021)	No mention found (focus on medication-related outcomes)	Yes
Tohashi et al., 2016	Prospective observational study with case-control elements	56 patients	No mention found	No mention found	No

Study Characteristics Analysis

- Study Design :
  - 4 studies used a retrospective design
  - 1 study was prospective with case-control elements
- Population :
  - We found varied population types across studies:
    - 1 study examined 6,742 procedures
    - 3 studies included a total of 576 patients
    - 1 study analyzed 18,421 MRONJ reports
- Follow-up Period :
  - We found follow-up periods for 4 studies, ranging from 3.5 to 17.75 years
  - We didn't find follow-up information for 1 study
- Procedures Studied :
  - Dental implants were the most common procedure, studied in 3 studies
  - Tooth extractions were examined in 2 studies
  - Periodontal procedures and removable prostheses were each studied in 1 study
  - We didn't find specific procedures mentioned for 2 studies

MRONJ Risk Analysis

Overall Incidence Rates

We found substantial variation in MRONJ incidence across studies, ranging from 0.03% in a large-scale procedure-based study to 57.14% in a smaller patient-based study. This variation appears to be influenced by factors such as study design, population characteristics, and the specific procedures examined.

- Penoni et al. (2023) reported a prevalence of 0.03% (2 cases out of 6,742 procedures) over a 9-year period.
- Kwack and Park (2023) identified 130 MRONJ cases out of 340 patients (38.2%).

- Pichardo et al. (2020) focused on 180 MRONJ patients but we didn't find an overall incidence rate in the abstract.
- Peng et al. (2022) analyzed 18,421 MRONJ reports but we didn't find an incidence rate calculation in the full text.
- Tohashi et al. (2016) reported 32 Antiresorptive agent-induced Osteonecrosis of the Jaw (ARONJ) cases out of 56 patients (57.14%).

Procedure-Specific Risks

Study	Procedure Type	MRONJ Cases	Time to Onset	Risk Factors
Penoni et al., 2023	Tooth extractions	1/1,568 (0.06%)	No mention found	Alendronate use >3 years
Penoni et al., 2023	Removable prostheses	1/2,139 (0.05%)	No mention found	Alendronate use >3 years
Kwack and Park, 2023	Dental extraction or implantation	130/340 (38.2%)	6 months post-surgery	Duration of medication, age, number of operated teeth, operation area
Pichardo et al., 2020	Dental implants	18/180 (10%)	Median 24 months (pre-existing implants), 6 months (new implants)	Peri-implantitis, implant insertion
Peng et al., 2022	No mention found	18,421 reports	Varies by medication and indication	Type of indication, specific drugs used
Tohashi et al., 2016	No mention found	32/56 (57.14%)	No mention found	Higher mandibular Bone Mineral Density (BMD) values

Analysis of Procedure-Specific Risks

- MRONJ Case Rates :
  - We found a wide range of MRONJ case rates across studies:
    - 2 studies reported rates <1% for specific procedures
    - 1 study reported a rate of 10% for dental implants
    - 2 studies reported rates >38% for various dental procedures
    - 1 study reported only the total number of cases without a percentage
- Time to Onset :
  - We found time to onset information for 3 studies:
    - 1 study reported 6 months post-surgery

    * 1 study reported median times of 24 months for pre-existing implants and 6 months for new implants
    * 1 study reported variable onset times depending on factors such as medication and indication

- Risk Factors :
  - We found risk factors for MRONJ in all 6 studies:
    * Medication-related factors (duration or type) were mentioned in 4 studies
    * Surgical factors were mentioned in 2 studies
    * Other factors mentioned in individual studies included age, dental conditions, medical indications, and bone density

Comparative Analysis

Anti-resorptive Medication Comparison

Study	Medication Type	Relative Risk	Onset Period	Patient Characteristics
Penoni et al., 2023	Bisphosphonates (Alendronate)	No mention found	>3 years	Elderly women (74 years)
Kwack and Park, 2023	Bisphosphonates, Denosumab, Romosozumab	No mention found	Mean 5.8 years (MRONJ group)	Female, age 55 years
Pichardo et al., 2020	No mention found	No mention found	No mention found	No mention found
Peng et al., 2022	Pamidronate, Zoledronic acid, Denosumab, Alendronate, Risedronate, Etidronic acid, Ibandronate, Romosozumab	Reporting Odds Ratio (ROR): 494.8 (Pamidronate) to 6.4 (Romosozumab)	Varies by medication and indication	>80% female for osteoporosis treatment
Tohashi et al., 2016	No mention found	No mention found	No mention found	No mention found

Analysis of Anti-resorptive Medication Comparison

- Medication Types :
  - We found information on medication types for 3 studies:
    * Bisphosphonates were mentioned in all 3 studies
    * Denosumab and Romosozumab were each mentioned in 2 studies
    * Other medications (e.g., Pamidronate, Zoledronic acid) were mentioned in 1 study
- Relative Risk :

  - We found relative risk information for 1 study, which reported a range of Reporting Odds Ratios from 494.8 to 6.4 depending on the specific medication

- Onset Period :
  - We found onset period information for 3 studies:
    * One reported >3 years
    * One reported a mean of 5.8 years
    * One reported that it varies by medication and indication

- Patient Characteristics :
  - We found patient characteristic information for 3 studies:
    * All 3 studies focused primarily on female patients
    * Age ranges varied, with one study specifically mentioning elderly women (74 years) and another including women aged 55 years

This analysis highlights the complexity of MRONJ risk assessment, with variations in medication types, onset periods, and patient characteristics across studies. The wide range of Reporting Odds Ratios found in one study suggests significant differences in MRONJ risk among different anti-resorptive medications, with Pamidronate showing the highest risk and Romosozumab the lowest. However, the limited number of studies reporting on each specific medication and the variability in study designs make it challenging to draw definitive conclusions about the comparative risks of different anti-resorptive medications.

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