Cohort Study

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Assessment of the occurrence of apical periodontitis and endodontically treated/non-treated teeth in a Lower Austrian patient population treated for osteoporosis: a cohort study

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Introduction: Osteoporosis (OP) is a bone disease linked to low bone mass and heightened fracture risk. Apical periodontitis (AP) is an inflammation of the apical periodontium, visible on radiographs, often associated with infection or necrosis of the root canal system. Both conditions, AP and OP, share inflammation and ageing as common factors, warranting exploration of their potential interactions. This study examined the association between AP and endodontically treated/non-treated teeth in patients with OP in Lower Austria.

Methods: The authors included 425 patients (7924 examined teeth) aged over 60 years (average age 68 ± 10 years) with 208 patients (3537 examined teeth) [179 women (3027 teeth) and 29 men (510 teeth)] initially diagnosed and treated for OP and a corresponding control group with 217 patients (4387 examined teeth) [187 women (3781 teeth) and 30 men (606 teeth)] without an OP diagnosis. For the diagnosis of AP, the panoramic radiographs and medical history taken at the initial presentation were analysed.

Results: In patients treated for OP, AP was diagnosed as follows: in 134 (26%) treated and 234 (9%) non-treated teeth among women (511 treated/2516 non-treated teeth) and in 23 (27%) treated and 50 (11%) non-treated teeth among men (83 treated/427 non-treated teeth). The control group without OP consisted of: women (569 treated/ 3212 non-treated teeth) in 147 (25%) treated and 403 (12%) non-treated teeth; men (77 treated/ 529 non-treated teeth) 17 (22%) treated and 29 (6%) non-treated teeth. When comparing AP in endodontically treated teeth according to sex, no statistically significant differences were observed between patients with and without OP ($P > 0.05$). The same result was observed in endodontically non-treated teeth ($P > 0.05$).

Conclusion: The authors' results indicate that there is no association between the occurrence of AP and endodontically or non-endodontically treated teeth in female and male patients treated for OP.

Keywords: bone diseases, cohort studies, osteoporosis, periapical periodontitis

Introduction

Osteoporosis (OP) is an age-related bone disease characterised by low bone mass and microarchitectural deterioration of the bone tissue, resulting in increased bone fragility and susceptibility to fracture[1]. This condition can markedly reduce quality of life, potentially resulting in severe disability or even death[2]. For a 50-year-old, the average lifetime risk of OP is estimated to be ~50% in women and 22% in men[3]. Postmenopausal women are most affected, with the risk increasing with age[4] due to decreased oestrogen levels and the concomitant increase in serum levels of pituitary follicle-stimulating hormone, which result in greater osteoclast-mediated bone resorption[5,6]. Depending on the factors affecting bone metabolism, OP is classified as primary OP, which includes postmenopausal (type I) and senile OP (type II), and secondary OP, which is influenced by preexisting diseases,

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medications, and lifestyle[7]. OP-specific treatment is generally recommended for individuals aged 50 years or older with a history of fragility fracture, particularly of the hip or spine. In addition, assessing the 10-year fracture probability using the country-specific (Austria) version of the fracture risk assessment tool (FRAX) is recommended. Similar to other countries, Austrian guidelines recommend OP treatment when the FRAX-based 10-year fracture probability is at least 20% for major osteoporotic fracture (MOF) or 5% for hip fractures[8].

A wide range of antiresorptive and osteoanabolic agents are available for OP treatment that aim to increase bone mineral density (BMD) and reduce the risk of fractures. The most commonly used drugs in Europe are bisphosphonates (BPs), denosumab (D), oestrogen, and selective oestrogen receptor modulators (SERMs)[9–11]. Over the past decade, reports have indicated an indirect association between OP and alterations in oral health. Low systemic BMD can be regarded as a risk factor for the progression of apical periodontitis (AP)[12,13]. Imaging procedures such as conventional radiography, focal plane tomography, and cone beam computed tomography (CBCT). have been used in study settings to evaluate potential OP[14]. Complex multistage measurements and calculations were performed in these studies.

AP is an inflammatory disease of the apical periodontium caused by infection or necrosis of the root canal system[15] and becomes visible after a period of time on two-dimensional and three-dimensional radiographs as a radiolucent field in the periapical bone compared to the surrounding healthy tissue structures[16–19]. The interpretation of radiological images relies on the ability of clinicians to visualise anatomical changes and relate them to specific biological processes[20]. It is estimated that endodontic diseases affect 7–86% of the population[21] and are the most common causes of pain of odontogenic origin[22,23]. The biological and therapeutic aims of endodontic treatment are either to prevent AP or to create optimal conditions for healing by removing infection, eliminating bacteria from the root canal system, and preventing re-infection[24]. Most periapical lesions (PAI) heal after careful non-surgical endodontic treatment[25]. A period of at least 6–12 months after root canal treatment should be considered to assess the healing potential[26].

Both AP and OP are bone diseases closely associated with inflammation and ageing. There are several common risk factors and correlations in their pathogenic mechanisms, prompting inquiries into the potential relationship between OP and AP[27].

Rodrigues *et al.*[28] also describe the prevalence of AP in OP patients in his 2024 review and Cadoni *et al.*[29], in their retrospective clinical study, describe a similar issue with the periapical status in OP patients, but with a smaller number of 76 patients.

We wanted to focus more on the endodontically/non-endodontically treated teeth and the AP by OA-treated patients with a larger number of cases.

This study aimed to investigate the relationship between AP and endodontically treated teeth in a population of Lower Austrian patients treated for OP.

Methods

The patient cohort comprised individuals referred to a dental outpatient clinic for treatment between November 2012 and November 2023.

HIGHLIGHTS

- The study explores osteoporosis (OP) prevalence and treatment impact, focusing on antiresorptive drugs.
- Findings reveal lower apical periodontitis (AP) prevalence in females with OP but higher in males.
- Recommendations include thorough dental screening for OP patients and improvements in root canal treatment to minimise complications.

Initially, all 2433 medical history forms for the patient cohort were screened. The patient cohort was then screened for medications, and patients for whom OP treatment was indicated were included. Ultimately, this study involved 208 patients (179 women and 29 men) originally diagnosed with OP. Further, 217 matched patients without OP (187 women and 30 men) who underwent dental evaluations within the same timeframe were selected as controls. The protocol for this study was reviewed by the Ethics Committee and was in accordance with the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards. This study was prepared in accordance with the STROCSS 2021 criteria[30].

Selection of cases

The inclusion criteria for the study group were as follows: being of Lower Austrian ethnicity; visiting the dental outpatient clinic since 2012; being male or female; undergoing treatment at the clinic; having an updated medical history; being aged over 60 years; having primary OP; undergoing treatment with (D), (BPs) (ORAL, IV, and IM), or vitamin D supplementation, or not undergoing treatment for OP; and having undergone X-ray and possessing the panoramic radiograph taken at the initial presentation. Written and oral histories were obtained to diagnose OP. Patients who were not in the selected age group, not undergoing treatment at our clinic, having an outdated or incomplete medical history, and having no panoramic radiographs were excluded. The control group comprised individuals who agreed to participate in the study but had no history of OP. They were randomly recruited from patients attending the dental clinic and matched as closely as possible for age, sex, and socio-economic status with patients with OP. Regarding socio-economic status, all patients were residents in Lower Austria at the time of treatment.

Clinical data collection

Written informed consent for the use of medical and dental charts was obtained from all patients. All medical records, including demographic data, medical history, and medications taken at the time of dental assessment, were examined, as well as whether the treatment was performed by a dentist. The parameters obtained from the dental screening were as follows: (a) AP, (b) root canal treatment, and (c) missing teeth. Each patient underwent a routine radiographic examination comprising at least one panoramic radiograph. All radiographs were obtained using a Dentsply Sirona Orthophos SL 3D imaging (Dentsply Sirona, Charlotte, USA) unit tube voltage: 60–90 kVp; tube current: 3–16 mA. The active sensor area measured 160 × 160 mm. Clinical applications typically use a field of view measuring ø5 × 5.5 cm, with radiation doses ranging from 3 to 20 μSv. All patients were positioned

according to the manufacturer's instructions using a 3-point fixating system, and a light device was used to determine the Frankfurt horizontal and mid-sagittal planes.

Acquisition of data

Medical history, diagnostic information, and treatment details for each patient were compiled. Additionally, all images from the first initial presentation were obtained and examined. The available data were used to calculate the prevalence of AP, root canal-treated teeth, missing teeth, and the arithmetic mean of the collected data. PAI were assessed on panoramic radiographs by four trained and experts in endodontics. Calibration was performed by the observers who assigned scores to the PAI twice at monthly intervals. For multirooted teeth, the highest scores assigned to the individual roots were used. In cases of disagreements between the four observers, the highest individual score was selected.

Statistical analysis

Data analysis was performed using Microsoft 365 Excel Version 2311 (Microsoft). The patient and control groups were divided based on sex and endodontic treatment initially and then further subdivided into groups with and without OP treatment.

Subsequently, these groups were analysed based on the percentage of AP per tooth that underwent endodontic treatment and statistically evaluated using SigmaPlot 13.0 (Systat Software Inc.) with a non-parametric Kruskal–Wallis one-way analysis of variance on ranks. Missing data were treated by mean imputation, where missing values were replaced by the average of the respective group. Outliers were identified by visual inspection and accounted for using robust statistical methods to minimise bias. In this study, 425 patients and 7924 teeth were examined (Fig. 1). In total, 366 women and 59 men were examined: 179 women and 29 men with OP and 187 women and 30 men without OP (Fig. 2). A total of 6808 and 1116 teeth of women and men, respectively, were examined. A total of 3027 teeth from women and 510 teeth from men with OP and 3781 teeth from women and 606 teeth from men without OP were examined (Fig. 4).

Of the 425 patients, 321 already had endodontically treated teeth. Of them, 281 were women and 40 were men. This resulted in 134 women and 23 men with OP having endodontically treated teeth. In contrast, 25 women and 6 men with OP had no endodontically treated teeth, while 40 women without OP and 13 men without OP had no endodontically treated teeth. A total of 1240 endodontically treated teeth were examined, 1080 in women and 160 in men. Of these, 594 were from patients with OP women: 511; men: 83) (Figs. 3–6).

Thus, 6684 teeth without endodontic treatment were examined in this study, of which 5728 belonged to women and 956 to men. A total of 2943 teeth without endodontic treatment were in patients with OP (women: 2516; men: 427) and 3741 (women: 3212; men: 529). These teeth were divided into four groups for statistical analysis: Group 1, teeth with endodontic treatment among women; Group 2, teeth without endodontic among women; Group 3, teeth with endodontic treatment among men; and Group 4, teeth without endodontic treatment among men. Each group was further subdivided into groups A (with OP) and B (without OP). The aim was to investigate whether there was a significant difference between groups A and B.

Results

The average age of the entire patient population (425 patients) was 68 ± 10 years. The 179 women with OP had the highest average age of 71 ± 9 years, the 187 women without OP had an average age of 66 ± 9 years, the 29 men with OP were on average 67 ± 11 years old, and the 29 men without OP were 70 ± 7 years old.

In women (366; 6808 teeth), the mean number of PAI per tooth in the group of teeth that had undergone endodontic treatment (Group 1, 281 women and 1080 teeth) was $33.5 \pm 35.5\%$ for those with OP (Group 1-A, 134 women and 511 teeth) and $39.8 \pm 31.0\%$ for those without OP (Group 1-B, 147 women and 569 teeth). In contrast, the mean number of PAI per tooth in the group of teeth that had not undergone endodontic treatment (Group 2, 85 women and 5728 teeth) was $6.8 \pm 8.1\%$ for those with OP (Group 2-A, 45 women and 2516 teeth) and $8.0 \pm 8.7\%$ for those without OP (Group 2-B, 40 women and 3212 teeth).

Among men (59; 1116 teeth), the mean number of PAI per tooth in the group of teeth that had undergone endodontic treatment (Group 3, 40 men and 160 teeth) was $38.7 \pm 28.1\%$ for those with OP (Group 3-A, 23 men and 83 teeth) and $16.8 \pm 23.2\%$ for those without OP (Group 3-B, 17 men and 77 teeth). In contrast, the mean number of PAI per tooth in the group of teeth that had not undergone endodontic treatment (Group 4, 19 men and 956 teeth) was $7.5 \pm 6.2\%$ for those with OP (Group 4-A, 6 men and 427 teeth) and $5.8 \pm 11.0\%$ for those without OP (Group 4-B, 13 men and 529 teeth).

No significant differences in the PAI were observed between women with and without OP, regardless of whether they received endodontic treatment (Fig. 7) or not (Fig. 8) ($P > 0.05$). The same result was observed in men in both subgroups ($P > 0.05$) (Figs. 9 and 10).

Additionally, no statistically significant differences were observed between patients with and without OP when comparing PAI on endodontically treated teeth by sex ($P > 0.05$). The same result was observed in endodontically non-treated teeth ($P > 0.05$).

Discussion

A considerable portion of the adult population (15% for persons aged ≥ 50 years) suffers from OP and receives or has received treatment with ARDs, mainly BPs and D. These drugs are also utilised for the management of other conditions such as primary or metastatic bone malignancies[31,32]. This study assessed and compared the periapical status in patients with OP treated with BPs or D, or given no treatment, with a control group of healthy individuals not on these medications. In women, the prevalence of AP was lower in those with OP than in healthy individuals (8.0% and 6.8% in non-endodontically treated teeth and 39.8% and 33.5% in endodontically treated teeth, respectively). Among men, the prevalence of AP was higher in patients with OP than in healthy individuals (5.8% and 7.5% in non-endodontically treated teeth and 16.8% and 38.7% in endodontically treated teeth). However, the number of teeth affected by AP was similar in all groups. Based on these results, no statistically significant differences were observed in the PAI between patients with and without OP. When considering OP alone, our findings closely align with the results of a cross-sectional clinical study with a similar sample size that identified a marginal association between

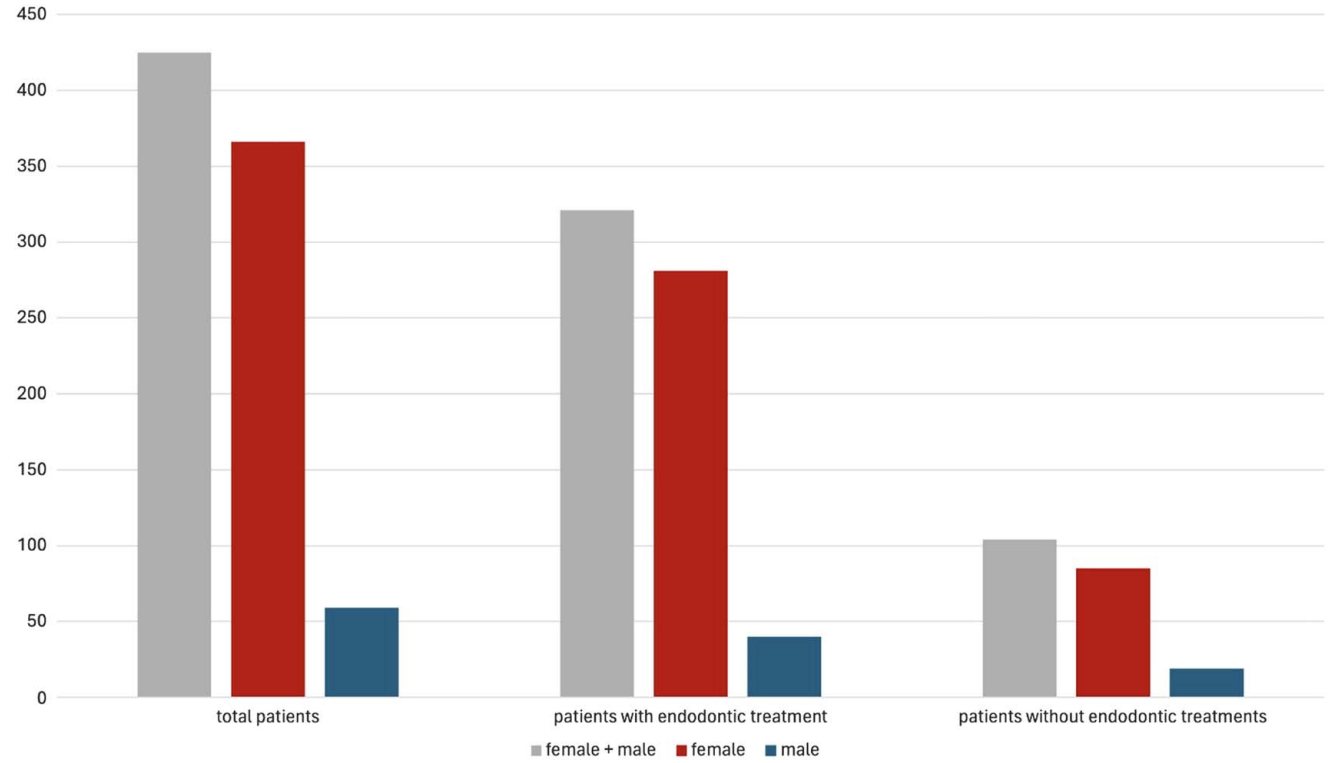

Figure 1. Graphical representation of the study cohort as a whole and subdivided into patients who had and had not undergone endodontic treatment.

lesions of AP in postmenopausal women and low mineral density conditions[33,34]. Our findings support the results of Cadoni *et al.*[29] who reported that surgery did not appear to be associated with AP development. The study by Cadoni and colleagues included a cohort of 76 patients with OP (8 men and 68 women), whereas we had a much larger patient cohort of 425 patients and 7924 teeth examined (366 women with 6808 teeth and 59 men with 1116 teeth). However, despite the large patient population, we were unable to establish a significant correlation between OP and AP.

Owing to the advanced age of the study group, certain patients had minor comorbidities, representing a potential limitation. The use of antiresorptive bone medications and BPs is constantly increasing in older adults; therefore, more focus should be given to patients with OPs in this subset of the population.

Despite careful conduction and analysis in this study, there are some limitations that should be considered. There is no exact correlation between a person's age and the number of teeth; however, we set the minimum age criterion as 60 years. The average age of the entire patient cohort was 68 ± 10 years. The

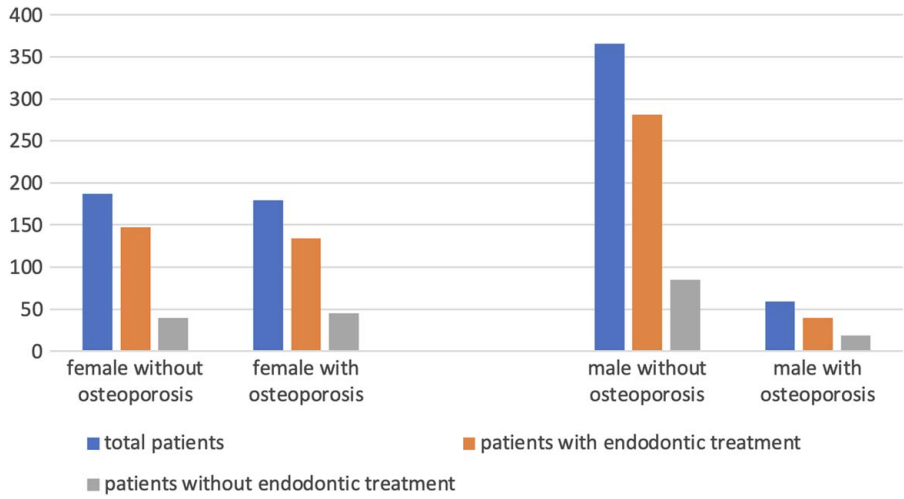

Figure 2. Graphical representation of the entire study cohort and the cohort subdivided into males and females with and without OP. OP, osteoporosis.

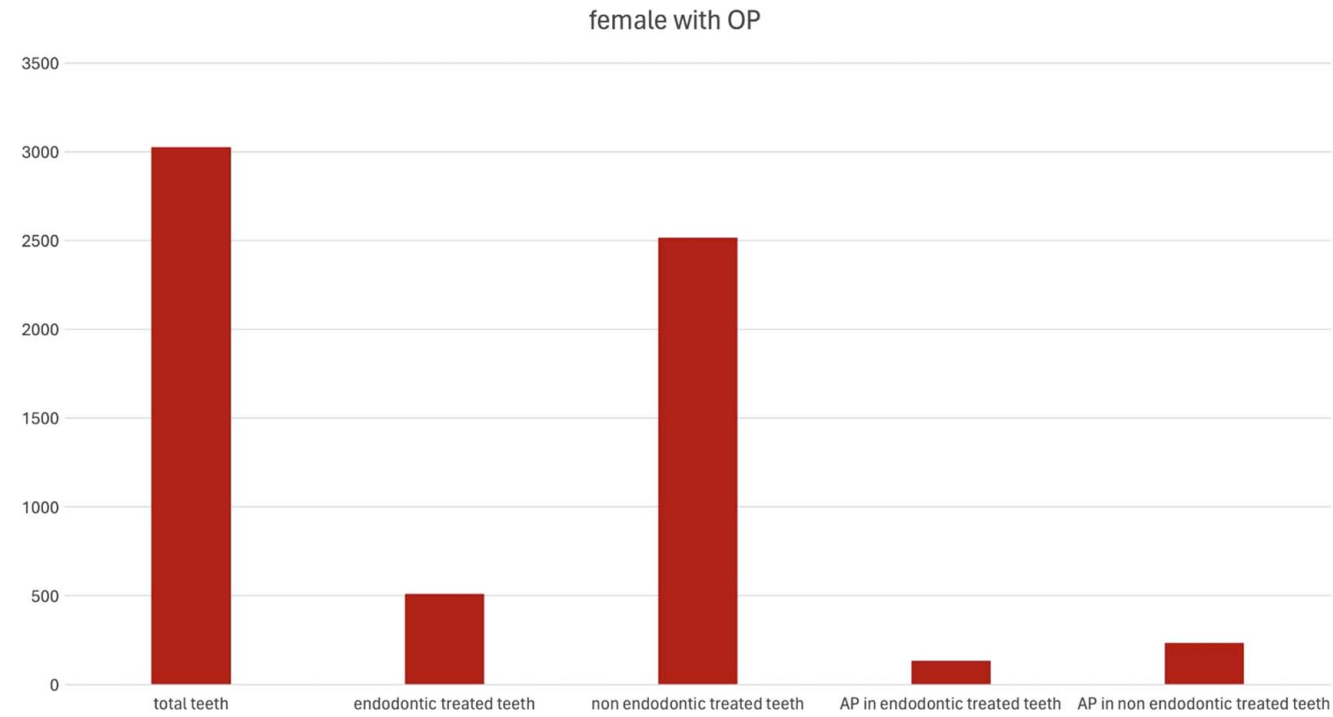

Figure 3. Graphical representation of all teeth of females with OP subdivided into teeth with and without endodontic treatment and with and without AP. AP, apical periodontitis; OP, osteoporosis.

exact type and duration of OP therapy was also not differentiated in the study. However, in this patient cohort, the use of D, BPs (ORAL, IV, and IM), or vitamin D supplementation, or lack of treatment, for OP were specified.

The exact relationship between the duration and type of treatment among patients with OP is still under investigation. However, our findings show that there is no significant difference between PAI in patients with OP of both sexes with either endodontically treated or non-endodontically treated teeth.

In addition, the aim of root canal treatment is to clean the root canals and reduce the bacterial load. Due to the complex anatomy of the root canal system, which can make complete cleaning

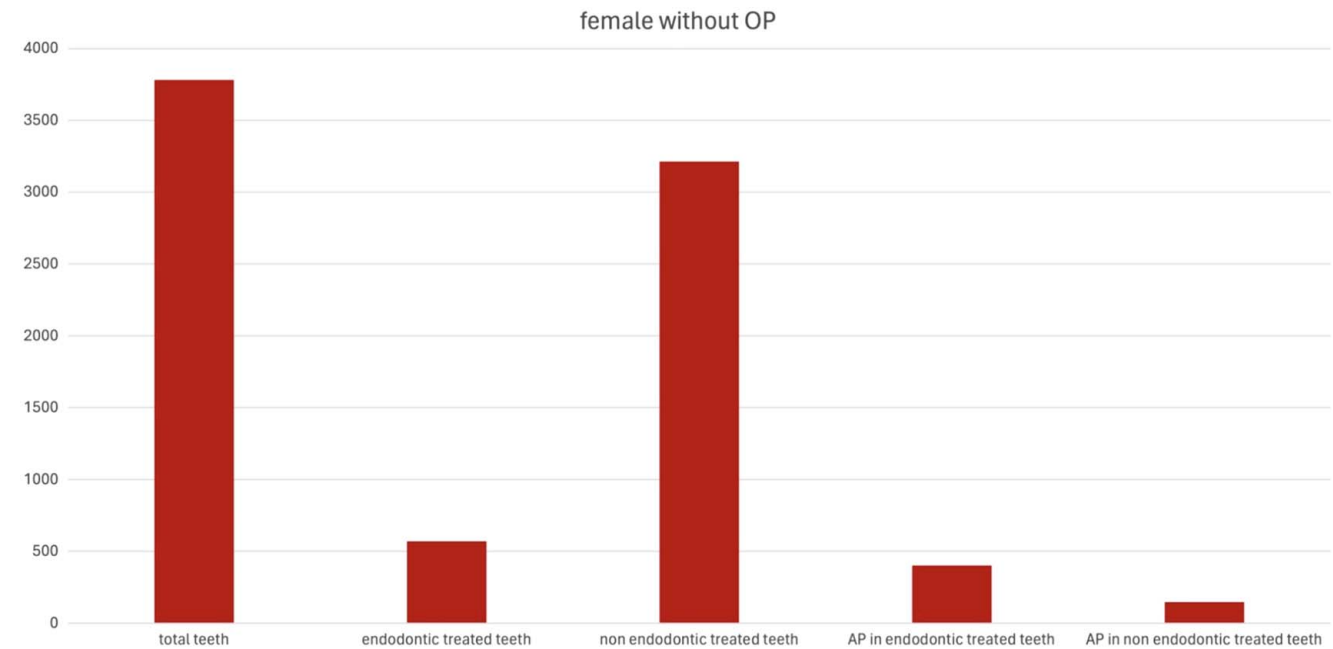

Figure 4. Graphical representation of all teeth of females without OP subdivided into teeth with and without endodontic treatment and with and without AP. AP, apical periodontitis; OP, osteoporosis.

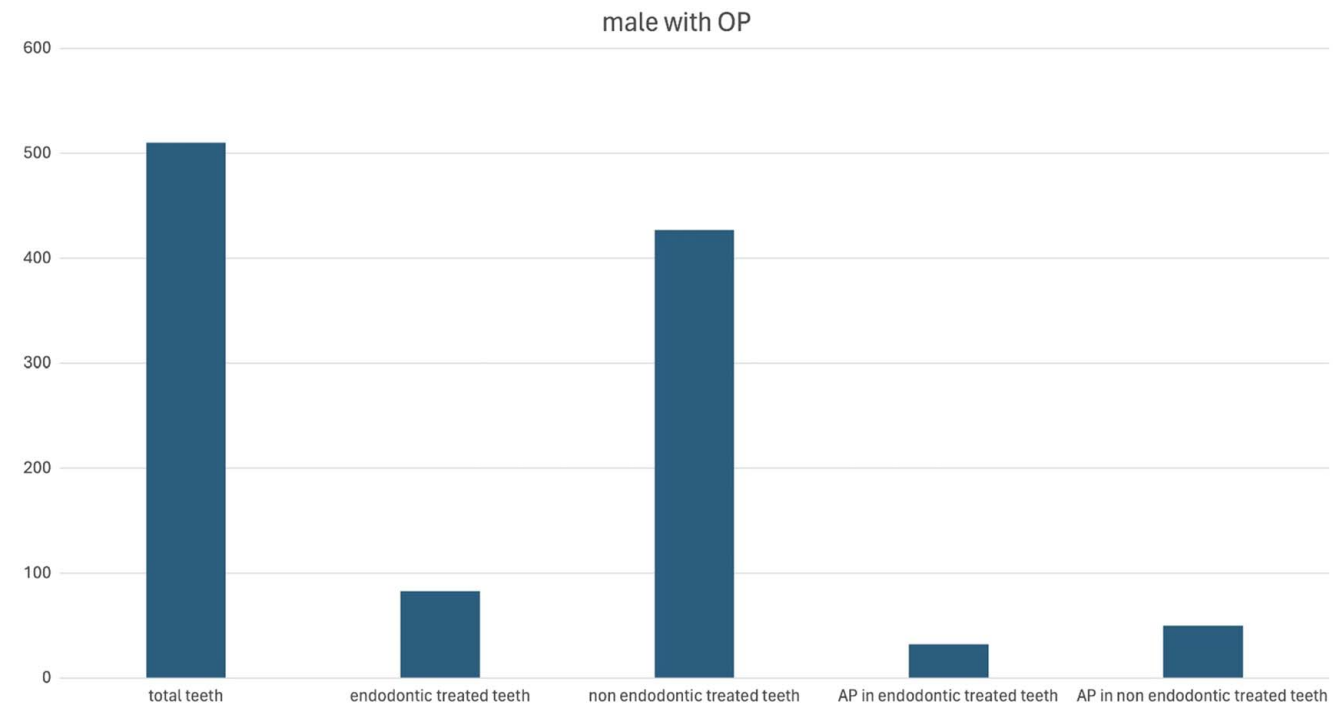

Figure 5. Graphical representation of all teeth of males with OP subdivided into teeth with and without endodontic treatment and with and without AP. AP, apical periodontitis; OP, osteoporosis.

difficult, inflammation may persist or recur after a few years, necessitating re-treatment[35]. In our study, the patients' radiographs were examined when they first presented to our clinic, and we lacked exact evidence of when the teeth were treated endodontically.

In addition to the type of root canal treatment (primary or secondary), the prognosis of endodontic healing is influenced by six other factors[36]: (1) the presence of preoperative radiolucency, (2) the presence of complicated operative factors (e.g. broken instruments or perforations), (3) the quality of the crown

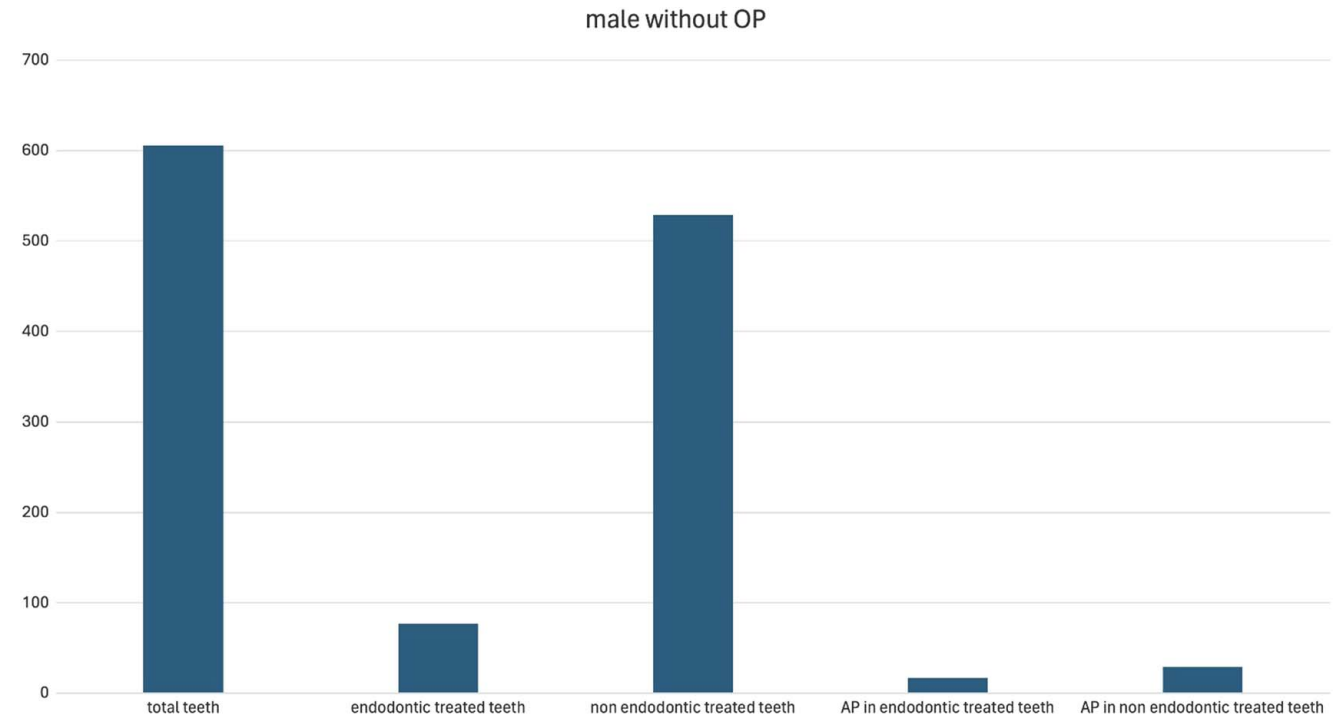

Figure 6. Graphical representation of all teeth of males without OP subdivided into teeth with and without endodontic treatment and with and without AP. AP, apical periodontitis; OP, osteoporosis.

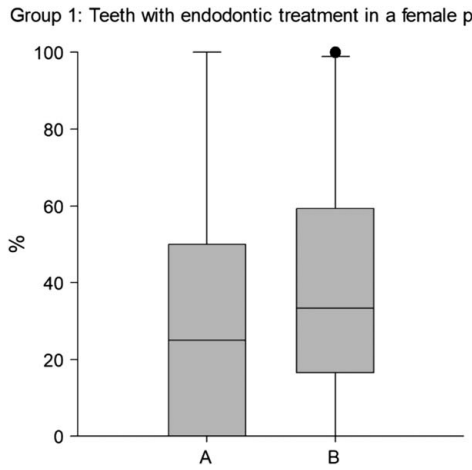

Figure 7. Teeth with endodontic treatment in female patients. Each group was divided again into A (with OP) and B (without OP). AP, apical periodontitis; OP, osteoporosis.

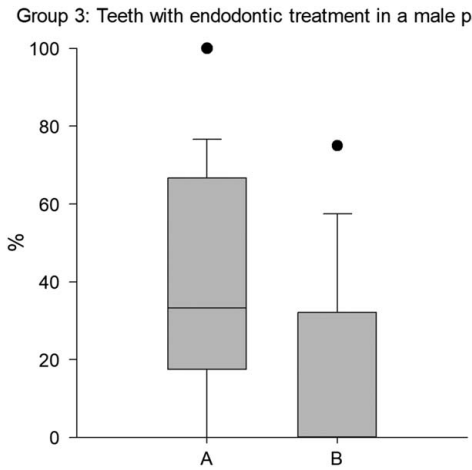

Figure 9. Teeth with endodontic treatment in male patients. Each group was divided again into A (with OP) and B (without OP). AP, apical periodontitis; OP, osteoporosis.

restoration, (4) the distance between the root canal filling and the radiological apex, (5) the preservation of the root canal morphology, and (6) the compactness of the root canal filling. The last three factors can be summarised as "technical quality" after endodontic treatment. A root canal treatment of good technical quality means that the canal filling was compact, ended within 0–2 mm of the apex, and had preserved morphology.

To assess the difficulty of endodontic treatment, guidelines for general practitioners have been developed: the Endodontic Treatment Classification Score (ETC)[37].

In our study, we focused only on the presence or absence of an AP. Final restoration and assessment of prognosis were not considered; however, we will consider these in future studies. Similarly, there were no specific inclusion and exclusion criteria based on ETC due to the increased difficulty of treatment after ETC.

Furthermore, we did not evaluate the differential diagnosis of different types of endodontic lesions, such as the prevalence and incidence of inflammatory changes like granulomas and periapical cysts due to root canal infection, by examining periapical biopsy specimens[38].

However, attempts to accurately assess the nature of periapical pathosis and diagnose the lesion prior to surgical intervention have been met with limited success. Although various methods are available, such as periapical radiographs[39], contrast media[40], Papanicolaou smears[41], real-time ultrasound imaging[42], and albumin tests[43], these have been shown to be inaccurate.

Another limitation of the study was that we assessed only radiological data and did not undertake a clinical examination of the teeth. Further, this study's reliance on periapical radiographs for the evaluation of the periapical status of teeth is a weakness.

These include a lower spatial resolution compared to more advanced imaging techniques such as CBCT. CBCT offers greater detail and the ability to visualise structures in three dimensions, which can significantly improve diagnostic accuracy.[44]

Figure 8. Teeth without endodontic treatment in female patients. Each group was divided again into A (with OP) and B (without OP). AP, apical periodontitis; OP, osteoporosis.

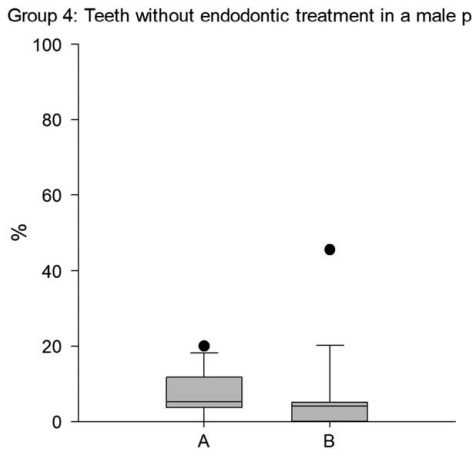

Figure 10. Teeth without endodontic treatment in male patients. Each group was divided again into A (with OP) and B (without OP). AP, apical periodontitis; OP, osteoporosis.

Despite these advantages, the use of advanced imaging techniques in this study was limited by several factors, as the standard procedure in our outpatient dental clinic was to obtain an OPTG as an overview image at the initial presentation. Despite the advanced imaging technology, a CBCT is less accessible, more expensive and often associated with a higher radiation dose compared to a panoramic radiograph.

Therefore, in this retrospective study, it was not possible to examine CBCT in all patients, as we included the presence of AP/OP at the time of initial presentation in our study. The comparison group with existing CBCTs at the first presentation would have been too small.

However, we plan to include CBCT in future studies to improve the diagnostic results and provide more accurate results for this research focus.

The lack of statistically significant differences in our study can be attributed to several possible factors. Firstly, it is important to consider the sample size and statistical power of the study. To our knowledge, we have the largest patient population in the literature corresponding to the topic of assessing the incidence of AP and endodontically treated/untreated teeth in patients with OP. In the future, we would like to see even larger numbers of cases in order to better recognise more precise results and possibly significant differences and to be able to provide even more definitive statements with larger samples. We also want to equalise the imbalance between the sexes. The prevalence in women and OP is simply significantly higher, but could be offset by higher case numbers, particularly in men. In addition, the variability within the data could mask potential differences. Biological variability, e.g. differences in individual response to dental or drug treatment, may contribute to this result. Standardisation of protocols and control of confounding variables may help to reduce this variability in future studies.

Additionally, none of the patients underwent hormone therapy with selective oestrogen receptor modulators or aromatase inhibitors. The design of this study poses limitations in establishing a causal relationship between the disease, medication use, and AP. AP is a multifactorial condition that complicates the assessment of all confounding factors influencing the disease[45]. This study's sample size was limited, emphasising the need for longitudinal studies with better control over variables such as medication, age, and comorbidities.

Although these limitations may affect the interpretation of the results, they do not diminish the importance of the associations identified. The results provide valuable insights and lay a solid foundation for future research in this area.

However, in light of our results, it is suggested that individuals with OP undergo thorough dental screening before initiating medication.

Particular attention should be paid during the dental examination to endodontic lesions and teeth that are not worth saving. Endodontic treatments and revisions can lead to extraction if not followed. Any necessary surgical tooth extraction or implantation should be carried out before starting drug therapy.

Additionally, efforts should be made to enhance the quality and outcomes of root canal treatment, which is the preferred option over tooth extraction, to minimise infection and medication-related osteonecrosis of the jaw[46].

Conclusion

Our findings show that OP was not associated with the development of AP. Further, there was no correlation between the occurrence of AP and endodontically treated teeth in patients who underwent surgery.

Additionally, no significant differences in PAI were observed between the sexes in non-endodontically treated teeth with and without surgery. Despite the limitations of this study, which preclude the generalisation of the results, the importance of the associations found is not diminished. The results provide valuable insight and a solid foundation for future research in this area and could be considered as further pieces of the puzzle in the field of AP.

Ethical approval

This study was approved by the responsible ethics committee of the province of Lower Austria (GS1-EK-4/520-2018).

Consent

The patients received a thorough explanation of this report and gave oral and written informed consent to be included in this study as well as for publication of anonymous data and pictures. A copy of the written consent is available for review on request.

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Author contribution

All authors contributed to the conception and design of the study; P.G., M.M., J.D., A.G., D.S., F.P.-M., S.H., M.G. and D.T. contributed to the data collection, analysis, and discussion of the data; P.G., M.M., J.D., A.G., D.S., F.P.-M., and D.T. wrote the manuscript; D.T. approved the final version to be published; All authors have read and approved the final version of the manuscript submitted for publication.

Conflicts of interest disclosure

The authors declare that there is no conflict of interest.

Research registration unique identifying number (UIN)

Not applicable.

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