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# Periodontitis and Its Role in Oral Cancer Susceptibility: A Case-Control Study

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## Abstract

**Introduction** Oral cancer and periodontitis are complex, multifactorial diseases, influenced by common risk factors such as genetic predisposition, lifestyle choices, and oral health practices. While certain studies indicate a positive correlation between periodontitis and oral cancer, the precise mechanisms and causation remain unclear.

**Objective** This study aims to determine if individuals with periodontitis have a heightened risk of developing oral cancer compared with those with healthy periodontal conditions.

**Materials and Methods** One hundred and twenty-six participants, 63 with oral cancer and 63 without oral cancer, were enrolled. A structured questionnaire was developed to gather data on demographics, socioeconomic status, lifestyle risk factors, dietary habits, periodontal condition, oral hygiene practices, and complete oral health status. Statistical analysis used chi-squared and Mann–Whitney *U* tests and logistic regression to understand potential influences on oral cancer development.

**Results** Notable associations were identified between oral cancer occurrence and specific socioeconomic factors and lifestyle behaviors, including gender, age, education level, and tobacco and alcohol usage. Average Silness and Loe plaque index values, probing pocket depth, and clinical attachment loss values were significantly higher in cases than controls. Patients with periodontitis exhibited a higher incidence of oral cancer (63.9%) compared with those without periodontitis (32.4%).

A substantial majority of oral cancer patients (72.9%) exhibited stage 4 periodontitis, contrasting with controls (30.6%).

**Conclusion** Periodontitis emerges as a significant individual risk factor influencing oral cancer development. Rigorous monitoring is recommended for individuals with compromised periodontal health, particularly with severe periodontitis and concurrent risk factors. Prioritizing preservation of periodontal health in high-risk individuals holds promise for mitigating oral cancer–associated risks.

**Keywords**
- periodontitis
- oral cancer
- risk factors
- chronic inflammation
- tobacco

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## Introduction

Periodontal diseases constitute a prevalent oral health issue affecting over 50% of the Indian population. While these conditions can impact individuals of all ages, their likelihood increases with advancing age.[1] The widespread occurrence of periodontal diseases poses an important public health challenge due to their adverse effects on oral health, including tooth loss, disability, aesthetic concerns, and masticatory issues. Moreover, these conditions can have systemic consequences and may contribute to undernourishment. The psychosocial and economic implications of periodontal diseases are substantial.[2] Many research studies have emphasized the connection between periodontitis and a range of systemic illnesses, such as diabetes, cardiovascular conditions, and adverse pregnancy outcomes. Furthermore, emerging evidence suggests a connection between periodontal disease and oral cancer (OC).[3]

Both periodontitis and OC share established risk factors, including smoking, tobacco use, alcohol consumption, poor oral hygiene (OH), unhealthy diet, age, systemic conditions like diabetes, autoimmune diseases, certain medications, bacterial infections, and genetic predisposition. Despite the shared risk factors contributing to both diseases, the specific mechanisms and their influence can vary.[4] Persistent inflammation in the mouth, frequently linked to periodontal conditions, is regarded as a separate risk factor for OC, as it can lead to deoxyribonucleic acid (DNA) damage, cell proliferation, and creation of a microenvironment conducive to the growth and survival of cancer cells. Furthermore, distinct risk factors and condition-specific elements play crucial roles in the onset and progression of each oral health issue. Recognizing these distinctions is crucial for the prevention, early detection, and effective management of gum disease and OC.[5] In this study, a reliable radiographic index (RI) assessing interproximal alveolar bone loss (iABL) in conjunction with clinical screening tools is included, providing a comprehensive approach to understanding the oral health status of individuals. The study aims to assess the association between periodontal disease and the potential risk of OC development within the population of Bengaluru city, India.

## Material and Methods

### Study Design

This study is a case-control study conducted in our in our faculty involving oral squamous cell carcinoma (OSCC) patients recruited from the department database between January 2020 and January 2024, based on histological confirmation.

### Inclusion Criteria

The study enrolled 126 participants (63 with OC and 63 controls) ranging in age from 18 to 90 years. Among them, 63 patients were in the case group, diagnosed with OSCC based on histological confirmation, and were recruited from the department database between January 2020 and January 2024. The control group consisted of 63 age- and sex-matched individuals without a history of OC, recruited from the outpatient section.

### Exclusion Criteria

Patients with cancers other than OSCC and patients with a history of jaw resection as a part of cancer therapy were excluded from the study.

### Questionnaire

A comprehensive questionnaire was designed to collect data on demographic information, socioeconomic status, risk factors, detailed dental and medical history, site of OC, and various parameters related to potential risk factors and confounding variables.

### Assessment of Dental and Oral Health

The decayed, missing, and filled teeth (DMFT) index was employed to evaluate dental health and the extent of dental caries. The Silness–Löe plaque index (SLPI) was utilized to assess OH status. Periodontal condition was evaluated through measurements of probing pocket depth (PPD) and clinical attachment loss (CAL) at six locations on each tooth. The average data for bleeding on probing (BOP) were subsequently computed. Periodontitis severity was categorized according to the criteria set forth by the World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions in 2018. Apart from the clinical evaluations, an RI was employed to assess the extent and severity of iABL relative to the lengths of individual roots. This approach utilized available panoramic radiographs to conduct a thorough assessment. Patients were briefed about the study's objectives, and written consent was obtained from all participants. The primary cancer-related treatment for the patients was managed appropriately. Referrals were made for any required conservative dental or periodontal treatment.

### Primary Outcome

The primary outcome of this study was to determine the association between periodontitis and OC susceptibility.

### Secondary Outcome

The primary outcome of this study was to assess the periodontal status and other oral health parameters (PPD, CAL, BOP percentage, SLPI, and DMFT index, radiographic assessment of alveolar bone loss) among individuals with OC compared with controls.

### Statistical Analysis

Statistical analysis was conducted using SPSS Statistics 18 software (IBM Corporation), utilizing the chi-squared and Mann–Whitney *U* tests and logistic regression. Statistical significance was determined at a *p*-value of less than 0.05.

### Ethical Statement

Ethics committee approval was obtained from the institutional ethics committee, dated January 4, 2020, with reference number EC 2020/PG/081. The procedures followed were

 

in accordance with the ethical standards of the responsible committee on human experimentation and with the Declaration of Helsinki 1964, as revised in 2013. Waiver of informed patient consent was obtained from the ethics committee.

## Results

Patients with periodontitis exhibited a higher incidence of OC (63.9%) compared with those without periodontitis (32.4%). A substantial majority of OC patients (72.9%) exhibited stage 4 periodontitis, contrasting with controls (30.6%). Significant associations were identified among age groups, education, tobacco use, alcohol consumption, and diet about case and control groups. The incidence of OSCC was higher among individuals older than 45 years compared with those younger than 45 years. The occurrence of OSCC was more among the patients/participants with lower levels of formal education as compared with patients/participants with higher education and employment. However, occupation and marital status did not prove to be significant factors. The calculated *p*-value of approximately 0.000102 for tobacco use strongly suggests a substantial association, indicating a connection between tobacco use and variations in the distribution of cases and controls. A total of 77.7% were current tobacco users among cases as compared with 38.5% among controls. Those who consumed more than 20 cigarettes or sachets of smokeless tobacco (SLT) per day exhibited elevated rates of OC. No significant correlation was found between passive smoking and the occurrence of OC. Percentage of daily alcohol consumption among cases was 56.79% as compared with 23.85% in controls. A notable correlation was observed between the incidence of OSCC and the quantity of alcohol consumption ($p = 0.027$; ►**Table 1**). In our study, excessive alcohol consumption emerged as an independent risk factor for the onset of OC.

Finally, diet was recognized as a likely factor influencing the distribution of cases and controls. The majority of OCs were found on the buccal mucosa (54%), followed by gingiva/gums (18%), tongue (11%), floor of the mouth (8%), labial mucosa (6%), and palate (3%). Analysis of dental status revealed that the case group had a higher proportion of

**Table 1** Comparison of demographic characteristics, socioeconomic risk factors, and lifestyle habits between the cases and control groups

| Variables | | Cases | Controls | *p*-value |
|---|---|---|---|---|
| Age (y) | >45 | 45 | 20 | < 0.001 |
| | < 45 | 18 | 43 | |
| Gender | Male | 36 | 36 | > 0.05 |
| | Female | 27 | 27 | |
| Education | Elementary school | 42 | 7 | < 0.05 |
| | High school | 14 | 20 | |
| | Degree | 7 | 36 | |
| Occupation | Employed | 18 | 27 | > 0.05 |
| | Unemployed | 12 | 9 | |
| | Home maker | 19 | 14 | |
| | Student | 1 | 1 | |
| | Retired | 13 | 12 | |
| Marital status | Single | 16 | 11 | > 0.05 |
| | Married | 30 | 39 | |
| | Widowed/divorced | 17 | 13 | |
| Tobacco | Smoking | 18 | 10 | < 0.05 |
| | Smokeless | 27 | 18 | |
| | Both | 4 | 0 | |
| | Never | 11 | 33 | |
| Alcohol consumption | Daily | 32 | 15 | 0.027 |
| | Weekly | 20 | 19 | |
| | Monthly | 4 | 9 | |
| | Never | 7 | 20 | |
| Diet | Vegetarian | 29 | 45 | 0.72 |
| | Nonvegetarian | 34 | 18 | |

 

**Table 2** Comparison of periodontal staging, CAL, PPD, BOP, RI (iABL), SLPI, DMFT INDEX between case and control groups

| Periodontitis stage | Cases | Controls | *p* value |
|---|---|---|---|
| I | 2 | 1 | $<0.05$ |
| II | 4 | 0 | $<0.05$ |
| III | 27 | 18 | 0.02 |
| IV | 27 | 5 | $<0.05$ |
| CAL (mm) | $6.2 \pm 1.3$ | $2.8 \pm 1.1$ | $<0.05$ |
| PPD (mm) | $5.6 \pm 1.3$ | $2.5 \pm 1.1$ | $<0.05$ |
| RI (iABL) | Codes 3 and 4 | Codes 2 and 3 | $<0.05$ |
| BOP (%) | $45.9 \pm 27$ | $27.9 \pm 18.9$ | $<0.05$ |
| SLPI | $2.7 \pm 0.9$ | $1.3 \pm 0.9$ | $<0.05$ |
| DMFT index | $24.7 \pm 9$ | $13.2 \pm 8.01$ | $<0.05$ |
| Completely edentulous | 6 | 3 | $>0.05$ |

Abbreviations: BOP, bleeding on probing; CAL, clinical attachment loss; DMFT, decayed, missing, and filled teeth; iABL, interproximal alveolar bone loss; PPD, probing pocket depth; RI, radiographic index; SLPI, Silness–Löe plaque index.

completely edentulous patients compared with the control group. The control group exhibited a significantly higher rate of filled teeth (F), whereas the case group had a higher rate of missing teeth (M). There was no significant difference in the number of decayed teeth (D) between the two groups. The mean DMFT value was $21.65 \pm 8.46$ in the case group and $14.18 \pm 8.26$ in the control group (►**Table 2**). A significant correlation was found between the occurrence of OC and periodontitis. The occurrence of OC was 57.1% among patients with periodontitis, whereas those without periodontal disease had a lower incidence of 26.6%. A significant correlation was identified, indicating that as the severity of periodontitis increased, there was a corresponding rise in the risk of OC development (►**Figs. 1** and **2**). The majority of OC patients, constituting 72.1% of the case group, were diagnosed with stage 4 periodontitis. In contrast, in the control group, most individuals had stage 2 periodontitis, accounting for 51.6%. Significant disparities were observed in the

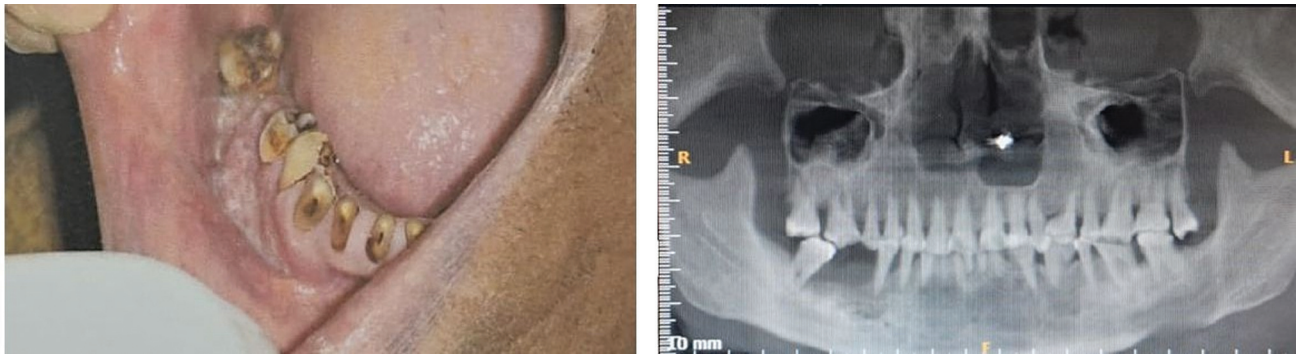


**Fig. 1** Clinical and radiographic image of a 54-year-old female patient with cancer of the lower right alveolus with no known risk factors apart from periodontitis.

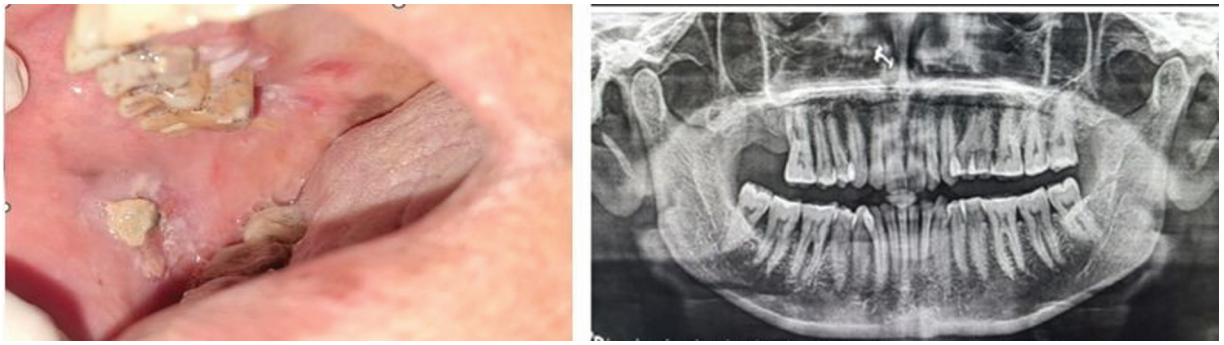

**Fig. 2** Clinical and radiographic images of a 36-year-old female patient with cancer of the upper right alveolus with no known risk factors other than periodontitis.

 

**Fig. 3** Clinical and radiographic images of a 48-year-old female patient with cancer of the lower right alveolus and the floor of the mouth with no known risk factors other than periodontitis.

mean values of CAL and PPD between the two groups. The case group demonstrated substantially higher values, with CAL at $6.2 \pm 1.3$, compared with $2.8 \pm 1.1$ in the control group. Similarly, the mean values of PPD and bleeding on probing percentage (BOP%) were higher among cases compared with controls. The RI (iABL) index scoring codes was 2 and 3 (moderate to severe alveolar bone loss) among controls (►**Figs. 3** and **4**) and 3 and 4 (severe to very severe alveolar bone loss) among cases (►**Figs. 1** and **2**). In the case group, there were more completely edentulous patients ($n = 6$) compared with the control group ($n = 3$). Among the completely edentulous patients, 11.3% were diagnosed with OC. Logistic regression analysis confirmed that the prevalence and severity of periodontitis were statistically significant factors.

## Discussion

India has the highest number of OC cases globally and is recognized as the global epicenter of this disease. Besides tobacco use, risk factors include the consumption of areca nut, alcohol, diet, human papillomavirus (HPV) infection, advancing age, male gender, and socioeconomic factors. Notably, periodontitis is also widespread in India, and both OC and periodontitis share common established risk factors like tobacco use, poor OH, etc.[6] Periodontitis is a persistent inflammatory condition that affects the supporting structures of the teeth, resulting in the deterioration of periodontal tissues leading to tooth mobility and tooth loss. It is known that the impact of periodontitis extends beyond the confines of the oral cavity, potentially giving rise to systemic consequences like diabetes, cardiovascular diseases, and cancer.[3] Although complex, evidence suggests a connection between periodontal disease and OC due to the considerable role of inflammation in both conditions.

In the present study, patients with periodontitis had a higher rate of OC (63.9%) compared with those without periodontitis (32.4%), and a large proportion of OC patients (72.9%) were diagnosed with stage 4 periodontitis, in contrast to just 30.6% of the control group. Five (7.9%) of the OC cases had severe periodontitis (stages III and IV) as their only identified risk factor. This finding underscores the potential unique contribution of periodontitis to OC susceptibility. The chronic inflammation associated with periodontitis may create an environment conducive to carcinogenesis, even in the absence of other major risk factors such as tobacco use, significant alcohol consumption, poor diet, or genetic predisposition.[7] Although 7.9% is a relatively small percentage, it is substantial in identifying periodontitis as a potential independent risk factor for OC. The present study confirms a significant correlation between OC and periodontitis, aligning with the findings of Javed et al's 2016 systematic review.[8] This highlights the importance of monitoring and managing periodontal health to potentially reduce the risk of OC in susceptible individuals.

The study also revealed that a notable number of individuals diagnosed with OC exhibited advanced periodontitis (stages III and IV), in stark contrast to the control group, which showed a lower prevalence of severe periodontitis. CAL was markedly elevated in cases of OC, as demonstrated by a substantially higher mean CAL of 5.7 mm, contrasting sharply with controls in whom the mean CAL was 2.7 mm. Likewise, PPD displays notable distinctions between cases (5 mm) and controls (2.2 mm). This considerable variance

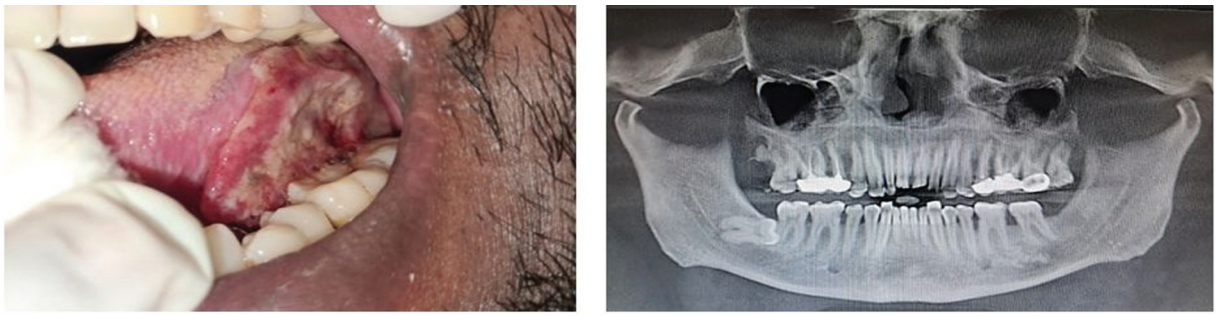

**Fig. 4** Clinical and radiographic images of a 40-year-old male patient with cancer of the left lateral border of the tongue and the floor of the mouth with no known risk factors other than periodontitis.

 

underscores the existence of more profound periodontal pockets among individuals with OC, highlighting the potential gravity of periodontal involvement in this cohort. The study demonstrates a distinct positive correlation between the severity of periodontitis and the prevalence of OC, consistent with the results of Komlós et al.[9] Severe periodontitis and OC may be linked through several mechanisms. Chronic inflammation caused by severe periodontitis can facilitate cancer development by leading to DNA damage and mutations. The development of a malignant lesion is often linked to inflammation, particularly due to oxidative damage to the cell's DNA.[10,11] Periodontitis is distinguished by increased levels of proinflammatory cytokines, acute phase proteins, and proteinases in the bloodstream.[12] Moreover, inflammatory mediators such as interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) found in periodontal lesions are linked to carcinogenesis.[13] Recent research indicates a direct connection between pathogens associated with periodontal disease and the onset of OC. Additionally, certain bacteria involved in periodontitis, such as *Porphyromonas gingivalis*, have been detected in higher levels in OC tissues, potentially contributing to cancer development.[14] Periodontal pockets could serve as reservoirs for cytomegalovirus, HPV, and Epstein–Barr virus, all of which are agents linked to OC.[15] This lends support to the hypothesis proposed by Sahingur et al, indicating that the severity of periodontitis and changes in the oral microbiome play a role in creating a favorable environment for the onset of OC.[9]

Shared risk factors, like tobacco and alcohol use, further complicate the relationship, as these can exacerbate both conditions. Poor OH associated with periodontitis may also delay OC detection as it may go unnoticed.[16] Thus, managing severe periodontitis and maintaining good oral health are crucial for reducing the risk of OC. Advanced periodontitis has the potential to compromise the local immune response, impacting the body's ability to regulate abnormal cell growth and potentially contributing to OC development. The proposition that periodontitis and OC may follow a sequential progression in certain cases is plausible, where severe periodontitis could serve as an early indicator or a contributing factor in the sequence of events leading to the development of OC.[17]

Radiographs, especially panoramic radiographs, facilitate precise assessment of the interproximal alveolar bone, aiding in the localization and measurement of bone loss. Radiographic indices like RI(iABL) facilitate the quantification of iABL.[18] The codes likely correspond to specific degrees of bone loss, allowing for a standardized and measurable assessment of severity. The RI (iABL) distribution shows a marked difference between cases and controls, with a higher prevalence of advanced iABL in OC patients, suggesting a potential link between OC and more severe bone loss. BOP is a common clinical indicator of periodontal inflammation, and its elevated levels among cases implies the need for attention to periodontal health in this population. The higher mean SLPI in cases, compared with controls, points to an increased level of dental plaque among OC patients. Elevated plaque levels not only impact the condition of the teeth and gums but also have systemic implications.[19] Consideration should be given to interventions aimed at improving OH and reducing plaque accumulation in OC patients to maintain overall oral health and potentially mitigate associated risks.

The observation that cases have a significantly higher mean DMFT index compared with controls indicates a higher prevalence of dental caries and tooth loss among individuals diagnosed with OC. Several factors could lead to the higher DMFT index observed in OC cases, including the effects of cancer treatments on oral health, potential alterations in salivary flow, and the presence of risk factors like tobacco use and inadequate OH. Additionally, there was a greater number of completely edentulous individuals among cases compared with controls, indicating a higher prevalence of complete tooth loss primarily associated with periodontitis among OC patients.

The findings of the study suggest that OC patients (cases) exhibit higher prevalence of periodontal conditions, including advanced periodontitis stages, higher CAL and PPD values, greater iABL, increased BOP, elevated SLPI, a higher DMFT index, and a higher rate of complete edentulism compared with the control group. These findings highlight the potential interplay between periodontal health and OC, emphasizing the relevance of comprehensive oral health assessments in patients.[20] It is important to note that while there is evidence suggesting a potential association, not all individuals with periodontitis develop OC, and the relationship is likely influenced by a combination of genetic, environmental, and lifestyle factors.[21,22]

This study offers novel insights into the association between periodontitis and OC, particularly within the Indian population, which experiences high rates of both conditions. It quantitatively establishes that individuals with periodontitis, especially in advanced stages, face a significantly higher risk of developing OC. The study integrates both clinical and radiographic evaluations to show that severe periodontitis is linked to increased OC risk, influenced by socioeconomic, lifestyle, and OH factors. It suggests that periodontitis may be an independent risk factor for OC, regardless of tobacco and alcohol use, and offers region-specific data to guide preventive strategies and further research.

## Conclusion

This study highlights the complex link between OC and periodontal health, showing that poor OH and plaque build-up create chronic inflammation that may promote OC development. The findings of this study support the notion that periodontitis is an independent risk factor for OC, with the risk increasing as periodontal disease progresses. Preventive measures for periodontal disease include regular dental visits and maintaining optimal OH. Dentists can contribute to reducing the risk of OC by evaluating and addressing patients' lifestyle and habits and monitoring compromised periodontal health. Further research and longitudinal studies are crucial to deepening our understanding of the intricate interplay between OC and periodontitis, laying the groundwork for more precise and effective preventive strategies in clinical practice.

Funding
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Conflict of Interest
None declared.

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