

A SYSTEMATIC REVIEW ON ASSOCIATION BETWEEN DENTURE-RELATED HABITS WITH ORAL POTENTIALLY MALIGNANT DISORDERS AND ORAL SQUAMOUS CELL CARCINOMA

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ABSTRACT

Background and Aim: Denture-related behavioral habits like poor denture hygiene, overnight wear, continuous use and prolonged denture use may be contributing factors for microbial biofilm formation, persistent *Candida* colonization, denture stomatitis and chronic oral mucosal inflammation. Chronic inflammation and *Candida* infection have been associated with mechanisms involved in oral carcinogenesis. This systematic review aimed to evaluate the association of denture-related behavioral habits with oral potentially malignant disorders (OPMDs) and oral squamous cell carcinoma (OSCC). **Methods:** A systematic review was performed according to the PRISMA 2020 guidelines. We conducted electronic database searches to identify relevant studies and screened them against pre-specified eligibility criteria. Results: A total of 159 records were identified, 87 were kept after duplicate removal, 36 full-text articles were assessed for eligibility, and six studies were included. The studies looked at denture habits, denture hygiene, *Candida* colonization, denture stomatitis and changes in the oral mucosa. The risk of bias was assessed by a modified Newcastle-Ottawa Scale. **Results:** Poor denture hygiene and persistent *Candida* colonization were consistently associated with denture stomatitis and chronic inflammatory changes. Some studies have reported leukoplakia and epithelial changes in denture wearers and denture wearing combined with tobacco smoking associated with oral candidal leukoplakia. However, no direct relationship of cause and effect was found between denture-related habits and OSCC. **Conclusion:** Poor denture-related habits are a contributing factor in denture stomatitis, persistent *Candida* colonization and chronic mucosal inflammation. There is no direct evidence linking these habits to oral cancer, but they may create an indirect environment that predisposes to potentially malignant changes, especially in the presence of established carcinogenic risk factors.

KEYWORDS: Dentures habits, Denture stomatitis, *Candida albicans*, Oral potentially malignant disorders, Oral squamous cell carcinoma.

INTRODUCTION

Increasing life expectancy and ageing of the population worldwide have resulted in a growing number of persons in need of removable dental prostheses for the rehabilitation of partial or complete edentulism. Although implant supported prostheses have advanced, removable dentures are still one of the most frequently used treatment options as they are inexpensive, simple to fabricate and restore mastication, speech and aesthetics adequately. The long-term success of removable dentures depends not only on the design and fabrication of the prosthesis but also on the behavioral habits of denture wearers, such as proper denture hygiene, regular replacement, periodic professional maintenance, and removal of dentures during sleep.¹

Denture related habits have appeared as major determinants of oral mucosal health. Behavior that are not favorable such as wearing dentures all the time, sleeping with dentures, improper cleaning, long use of old dentures and skipping of routine dental care, all contribute to the buildup of denture plaque and microbial biofilms. These behaviors facilitate colonization of the skin by *Candida albicans* and other microbes, which can lead to denture stomatitis and chronic mucosal inflammation.^{2,3} Denture stomatitis is one of the most frequent oral lesions in denture wearers, with a prevalence ranging from 15% to 70%, depending on the population studied and the diagnostic criteria used.⁴

Denture stomatitis is a chronic inflammation of the mucosa covered by removable dentures. It is considered a multifactorial disease. Although *Candida albicans* is thought to be the main etiological agent, continuous denture use, poor denture hygiene, decreased salivary flow, systemic diseases including diabetes mellitus, smoking, and immunosuppression greatly increase the risk of the disease.⁵ Prolonged use of dentures, particularly during sleep, reduces the cleansing ability of saliva and creates a moist anaerobic environment under the denture base, which promotes the formation of mature microbial biofilms. Therefore, persistent fungal colonization and recurrent inflammation may occur, especially in elderly denture wearers.⁶

There is accumulating evidence that chronic inflammation plays an important role in carcinogenesis. Chronic inflammatory responses induce the secretion of pro-inflammatory cytokines, reactive oxygen species (ROS), reactive nitrogen species (RNS), matrix metalloproteinases and angiogenic factors leading to oxidative DNA damage, increased epithelial cell proliferation, inhibition of apoptosis and genomic instability.⁷ Chronic inflammations have thus been identified as one of the enabling characteristics of cancer development and progression.

In addition to inducing chronic inflammation, *Candida albicans* has been implicated in several biological mechanisms involved in oral carcinogenesis. Experimental and clinical studies have demonstrated that some species of *Candida* can produce carcinogenic metabolites (e.g. acetaldehyde and nitrosamine-like compounds) that can induce DNA damage and promote epithelial dysplasia. Moreover, oral leukoplakia, chronic hyperplastic candidiasis and other oral potentially malignant disorders (OPMDs) have often been associated with chronic candidal infection, implying that long-standing fungal colonisation may induce malignant transformation in predisposed individuals.^{8,9}

Although a number of studies have demonstrated the association of poorly fitting dentures and chronic mechanical irritation as possible co-factors in oral carcinogenesis, relatively little attention has been paid to denture-related behavioral habits as independent or contributory risk factors. Wearing dentures overnight, poor denture hygiene, wearing dentures for long periods of time and not removing them while sleeping are common habits, but are largely preventable. These habits are conducive to the development of denture stomatitis and chronic *Candida* colonization, which in turn facilitates the development of a chronic inflammatory state that may enhance susceptibility to OPMDs and oral squamous cell carcinoma (OSCC), particularly when combined with established carcinogens such as tobacco, alcohol use, and betel quid chewing.¹⁰

Current evidence indicates a biologically plausible link between poor denture habits and oral carcinogenesis. The literature on this topic is fragmented and most studies have focused on isolated aspects, such as denture stomatitis, *Candida* infection or chronic inflammation. To date, no review has comprehensively synthesized denture-related behavioral habits as potential contributors to OPMDs and oral malignancies. This systematic review aims to evaluate and summarize the existing evidence for an association between denture-related behavioral habits, such as overnight denture wear, continuous denture use, poor denture hygiene, prolonged denture use, and denture stomatitis, and the development of potentially oral malignant disorders and oral squamous cell carcinoma.

METHODOLOGY

STUDY DESIGN

This systematic review will be conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Statement. The review protocol will be developed following the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) guidelines.

Research Question

The review aims to answer the following research question:

"Is there an association between denture-related behavioral habits and the development of oral potentially malignant disorders (OPMDs) and oral squamous cell carcinoma (OSCC)?"

The research question is based on the PECO framework:

- **Population (P):** Adults (≥ 18 years) wearing removable complete or partial dentures.
- **Exposure (E):** Denture-related behavioral habits, including overnight denture wear, continuous denture use, poor denture hygiene, inadequate denture cleaning, prolonged denture use, failure to remove dentures during sleep, prolonged use of old dentures, irregular denture replacement, and denture stomatitis associated with these behaviors.
- **Comparison (C):** Individuals with recommended denture hygiene practices or without the exposure of interest.
- **Outcome (O):** Oral potentially malignant disorders (leukoplakia, erythroplakia, oral epithelial dysplasia, chronic hyperplastic candidiasis, oral submucous fibrosis where applicable) and oral squamous cell carcinoma.

ELIGIBILITY CRITERIA

Inclusion Criteria

- Original research articles.
- Observational studies, including cohort, case-control, and cross-sectional studies.

- Clinical studies evaluating denture-related behavioral habits.
- Studies reporting oral potentially malignant disorders and/or oral squamous cell carcinoma as outcomes.
- Studies published in English.
- Full-text articles available.

Exclusion Criteria

- Case reports and case series involving fewer than five patients.
- Narrative reviews, systematic reviews, editorials, commentaries, conference abstracts, and letters to the editor.
- Animal or in vitro studies.
- Studies evaluating only ill-fitting dentures or mechanical trauma without assessing denture-related behavioral habits.

Information Sources

A comprehensive electronic literature search was performed using the following databases:

- PubMed/MEDLINE
- Scopus
- Web of Science
- Embase
- Cochrane Library

Additionally, manual searches of the reference list of included studies and relevant reviews will be conducted to identify eligible studies not retrieved through electronic searches.

Search Strategy

The search strategy will combine Medical Subject Headings (MeSH) and free-text keywords using Boolean operators.

PubMed search strategy:

("Denture"[Mesh] OR denture* OR removable prosthesis OR complete denture OR partial denture)

AND

("Night-time wear" OR overnight wear OR continuous wear OR denture hygiene OR denture cleaning OR denture cleansing OR denture habits OR denture stomatitis OR Candida OR denture plaque)

AND

("Oral potentially malignant disorders" OR leukoplakia OR erythroplakia OR epithelial dysplasia OR oral precancer OR oral cancer OR oral squamous cell carcinoma OR OSCC)

Search strategies were modified appropriately for each database.

Risk of Bias Assessment

This systematic review's methodology adhered to the Cochrane database of systematic reviews, and the bias analysis of the articles was created using a modified version of the Newcastle–Ottawa Scale for cross-sectional studies.¹¹ This modified version of the Newcastle–Ottawa Scale assesses study quality based on selection which included sample representation, sample size, non-respondents, and risk factors comparability, and outcome measurement which included assessment of outcome and statistical test.

RESULTS

The study selection process is illustrated using a PRISMA 2020 flow diagram.¹²

Figure 1: PRISMA 2020 flow diagram for newly conducted systematic reviews that solely involved database and registration searches

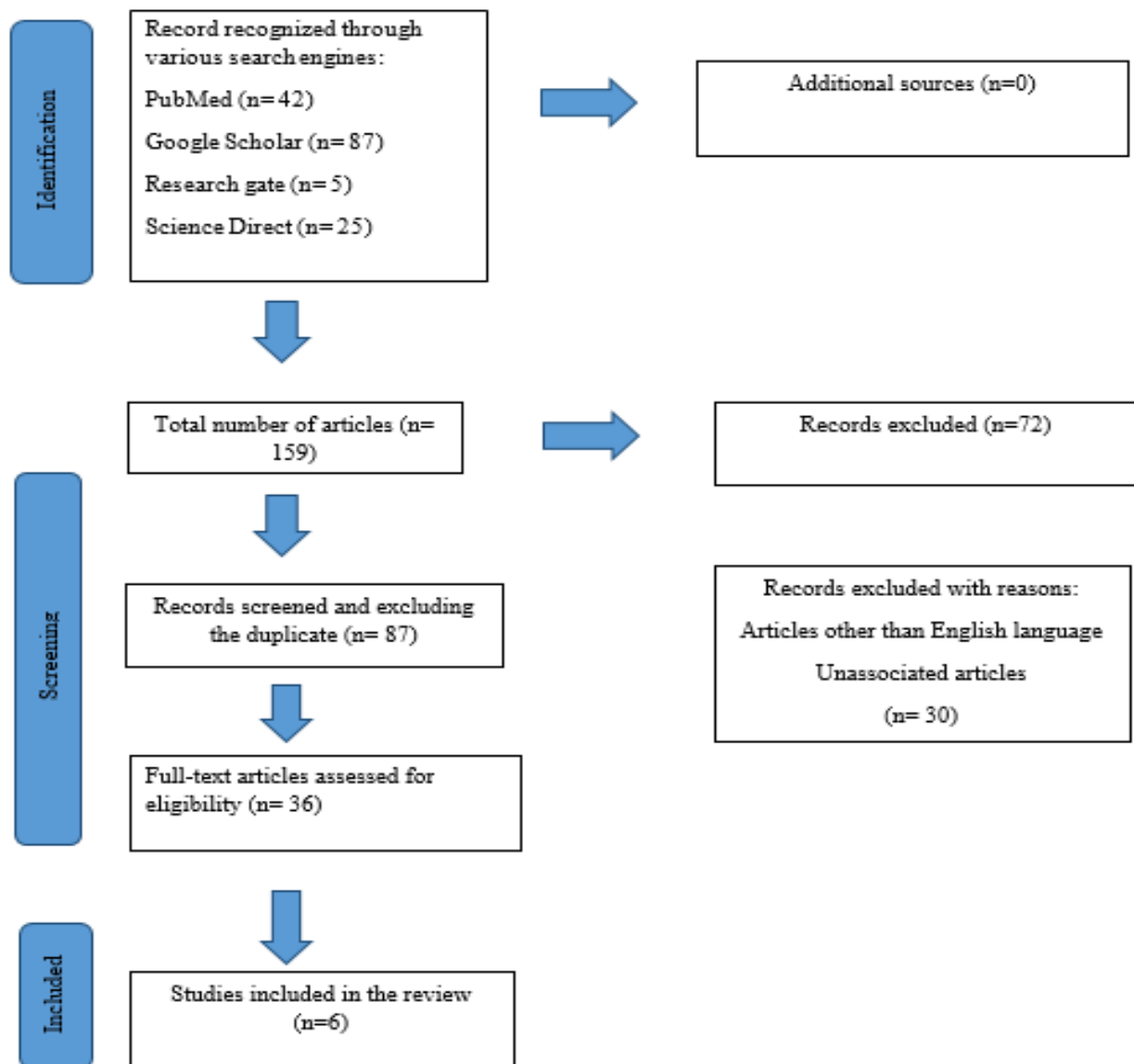


Figure 1 shows PRISMA Flow diagram showing the number of studies identified, screened, assessed for eligibility, excluded and included in the systematic review

TABLE 1: CHARACTERISTICS OF THE INTERVENTIONS IN THE INCLUDED STUDIES.

S.No	Author	Year	Patient Selection	Study Design	Intervention / Exposure
1	Arendorf TM et al. ¹³	1983	Patients diagnosed with oral candidal leukoplakia	Case-control	Investigated denture wearing and tobacco smoking as associated factors in oral candidal leukoplakia.
2	Bergendal T, Isacson G ¹⁴	1983	48 patients with denture stomatitis and 24 healthy denture wearers	Cross-sectional	Clinical, mycological, and histological evaluation of denture stomatitis, yeast growth, and oral mucosal changes.
3	Budtz-Jørgensen E et al. ¹⁵	1990	10 patients with chronic denture-induced stomatitis	Cross-sectional study	Histological, microbiological, and hematological evaluation of chronic denture-induced stomatitis.
4	Kulak Y, Arikan A ¹⁶	1993	75 complete denture wearers (15 localized DS, 45 generalized DS, 15 controls)	Cross-sectional	Evaluated overnight denture wearing, denture hygiene, smoking, denture brushing frequency, denture age, and <i>Candida</i> colonization.

S.No	Author	Year	Patient Selection	Study Design	Intervention / Exposure
5	Sakki TK et al. ¹⁷	1997	780 adults (452 complete denture wearers), Finland	Cross-sectional population study	Assessed denture hygiene, lifestyle, smoking, alcohol, salivary flow, denture retention, and denture stomatitis.
6	Naik AV, Pai RC ¹⁸	2011	100 complete denture wearers (70 with stomatitis, 30 controls)	Cross-sectional	Evaluated denture hygiene, denture age, salivary flow, and <i>Candida</i> colonization.

Table 1 presents the characteristics of the studies included in the systematic review. All six studies examined the role of how denture related habits influenced the oral mucosa. However, the studies differed in terms of patient age, sample size, and the duration of outcome assessment.

TABLE 2: CHARACTERISTICS OF THE PRIMARY OUTCOME AND RESULTS OF THE STUDIES INCLUDED IN THE SYSTEMATIC REVIEW

S.No	Author	Year	Outcome	Result
1	Arendorf TM et al. ¹³	1983	Association between denture wearing and candidal leukoplakia	Denture wearing, especially when combined with tobacco smoking, was associated with oral candidal leukoplakia, suggesting a possible role in potentially malignant lesions.
2	Bergendal T, Isacson G. ¹⁴	1983	Histological changes seen in denture stomatitis	Hyperplastic lesions showed greater yeast growth; leukoplakia and chronic inflammatory changes were observed in some denture wearers.
3	Budtz-Jørgensen E et al. ¹⁵	1990	Histopathological changes in chronic denture stomatitis	Chronic denture stomatitis demonstrated inflammatory epithelial alterations with variable tissue responses related to microbial colonization.
4	Kulak Y, Arikan A et al. ¹⁶	1993	Risk factors for denture stomatitis	Poor denture hygiene, smoking, and <i>Candida</i> colonization were significantly associated with denture stomatitis, whereas overnight denture wear and brushing frequency were not statistically significant.
5	Sakki TK et al. ¹⁷	1997	Association between behavioral factors and denture stomatitis	Poor oral hygiene and unhealthy lifestyle were significantly associated with denture stomatitis; salivary yeasts were associated with biologic factors.
6	Naik AV, Pai RC et al. ¹⁸	2011	Factors contributing to denture stomatitis	Poor denture hygiene and increased <i>Candida</i> colonization were the strongest contributors; denture age influenced fungal colonization more than inflammation.

Table 2 shows the outcome and result of the studies mentioned above. The outcome and results were significant, indicating that denture habits plays a crucial role in developing denture stomatitis. Poor denture hygiene was associated with increased risk of denture stomatitis and candidal leukoplakia, suggesting a possible role in potentially malignant lesions.

TABLE 3: BIAS ANALYSIS OF THE INCLUDED STUDIES

Author	Sample Representation	Sample Size	Ascertainment of Exposure	Risk Factors (Confounders Identified)	Comparability	Assessment of Outcome	Statistical Test
Arendorf TM et al. ¹³	*	—	*	*	*	*	*
Bergendal T, Isacson G et al. ¹⁴	*	*	*	*	—	*	*
Budtz-Jørgensen E et al. ¹⁵	*	—	*	*	—	*	*
Kulak Y, Arikan A et al. ¹⁶	*	*	*	*	*	*	*

Author	Sample Representation	Sample Size	Ascertainment of Exposure	Risk Factors (Confounders Identified)	Comparability	Assessment of Outcome	Statistical Test
Sakki TK et al. ¹⁷	*	*	*	*	*	*	*
Naik AV, Pai RC et al. ¹⁸	*	*	*	*	*	*	*

*indicates **low risk of bias** (criterion satisfied); – indicates **high or unclear risk of bias** (criterion not satisfied).

Interpretation of Bias Analysis

Sakki et al. (1997)¹⁷ demonstrated the **lowest risk of bias**, fulfilling all assessment criteria because of its large population-based sample and appropriate statistical analysis. **Kulak et al. (1993)**¹⁶ and **Naik & Pai (2011)**¹⁸ also showed a **low overall risk of bias**, with well-defined populations, standardized exposure assessment, and appropriate outcome evaluation. **Bergendal & Isacson (1983)**¹⁴ had a slightly higher risk of bias due to limited adjustment for confounding variables, while **Arendorf et al. (1983)**¹³ received a lower rating for sample size because it was a case-control study with a relatively small study population. **Budtz-Jørgensen et al. (1990)**¹⁵ had the highest risk of bias among the included studies, primarily because of its small sample size and limited control of confounding factors.

DISCUSSION

The present systematic review was aimed at evaluating the available evidence regarding the influence of denture-related habits on the development of oral mucosal alterations, with particular reference to their possible role in oral potentially malignant disorders (OPMDs). Although the studies included did not establish a direct causal relationship between denture habits and oral squamous cell carcinoma (OSCC), they consistently showed that poor denture hygiene, long-term denture use, and persistent *Candida* colonization are strongly associated with denture stomatitis and chronic inflammatory changes of the oral mucosa. Our findings suggest that denture-related habits may contribute indirectly to oral carcinogenesis through the induction of chronic inflammation and microbial dysbiosis, rather than acting as independent carcinogens.

Nikawa et al. reported that poor denture hygiene leads to microbial accumulation on denture surfaces and plays an important role in chronic mucosal inflammation, highlighting the significance of effective denture cleansing in the prevention of denture-associated lesions.¹⁹ Similarly, **Ramagie et al.** showed that *Candida* biofilms on denture acrylic are more resistant to antifungal agents and host immune responses and thus contribute to persistent infection and recurrent denture stomatitis.²⁰ These observations support the present review, in which poor denture hygiene was the most consistent behavioral risk factor among the studies included.

The main biological mechanism that links denture-related habits with potentially malignant changes of the oral mucosa appears to be persistent *Candida* colonization. Chronic infection with *Candida* not only leads to a sustained inflammatory response, but also causes epithelial damage due to the release of hydrolytic enzymes, proteinases, phospholipases and other virulence factors.

Webb et al. pointed out that *Candida*-associated denture stomatitis is not caused by fungal infection alone but is the result of a complex interaction between microbial biofilms, host susceptibility and local environmental factors.³ The prolonged wearing of dentures, poor oral hygiene and inadequate prosthesis care all favour chronic colonization and repeated epithelial lesions.

Several experimental studies have suggested additional mechanisms by which *Candida albicans* may contribute to oral carcinogenesis. **Gainza-Cirauqui et al.** demonstrated significantly higher levels of acetaldehyde production by *Candida* isolates from oral potentially malignant disorders. Acetaldehyde is a well-known carcinogenic metabolite that can cause DNA damage and epithelial dysplasia.²¹ Likewise, some *Candida* strains have been proposed to have nitrosation potential, which would enable the endogenous production of nitrosamines, potentially increasing carcinogenic activity in the oral cavity.²⁵ These mechanisms are mostly experimental, but they provide biological plausibility for the indirect association observed between chronic infection with *Candida* and malignant transformation.

Feller et al. have also supported this review, who suggested that chronic oral candidiasis should be considered as a promoter rather than an initiator of oral carcinogenesis. Persistent inflammatory stimulus and carcinogenic products from a chronic fungal infection can result in epithelial dysplasia especially in patients with predisposing factors such as tobacco, alcohol, immunosuppression or nutritional deficiencies.²² Similarly, **Di Cosola et al.** reported that *Candida albicans* contributes to oral carcinogenesis through chronic inflammation, oxidative stress, pro-inflammatory cytokines and acetaldehyde production, but the present evidence is not enough to establish a direct causal relationship.²³

Meera et al. reported that aspirin influences cancer-related pathways through modulation of COX-dependent signaling, PGE₂ production, platelet activity, and immune responses, thereby affecting apoptosis, tumour progression and metastasis. Similarly, denture-related habits may contribute to persistent local irritation and inflammatory changes in the oral mucosa, which could potentially facilitate processes involved in oral

carcinogenesis. Despite differences in the nature of the exposures, both highlight the potential role of inflammation and altered cellular signaling in tumour development and progression.

Despite the consistent association between denture-related habits and denture stomatitis, the present review further highlights important limitations of the available evidence. Most of the studies included had cross-sectional designs, hence temporal relationships could not be evaluated and causality could not be inferred. Study populations, methods of evaluation of denture hygiene, diagnostic criteria for denture stomatitis and assessment of *Candida* colonization were considerably heterogeneous. In addition, important confounding factors, such as smoking, alcohol consumption, systemic diseases, xerostomia, denture fit and duration of denture use, were not consistently controlled for in the studies. These methodological limitations introduce uncertainty into the total body of available evidence and help explain why there is no direct clinical evidence linking denture-related habits to oral malignancy.

CONCLUSION

In conclusion, the findings of this review supports the view that poor denture hygiene and prolonged denture use are major contributing factors to denture stomatitis and chronic *Candida* colonization. While there is no direct causal relationship with oral malignancy, these behaviours produce a chronic inflammatory environment that may allow for malignant transformation in the presence of established carcinogenic risk factors.

Since denture related behavioural factors are largely modifiable, emphasis should be placed on improving patient education about denture hygiene, overnight denture removal, regular prosthesis replacement and periodic professional review. Early diagnosis and effective management of denture stomatitis may reduce chronic mucosal inflammation and persistent *Candida* colonization and thereby limit biological conditions that may predispose to epithelial dysplasia in susceptible individuals.

Future studies should be based on well-designed prospective cohort studies with standardized definitions of denture-related habits, objective assessment of microbial colonization and long-term follow-up to see if chronic denture stomatitis is an independent risk factor for OPMDs or oral squamous cell carcinoma. Such studies should adjust for major confounding variables adequately to better define the contribution of denture-related habits to oral carcinogenesis.

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