

# PERIODONTITIS AS A POSSIBLE CAUSE OF CHRONIC HEART FAILURE

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## Abstract

**Background.** The objective of this study was to investigate the prevalence of periodontitis in patients with chronic heart failure, as well as to characterize the microbiological profile of periodontitis across different chronic heart failure phenotypes. The objective is to analyze the link between oral health and heart disease.

**Materials and Methods.** A cohort of 98 chronic heart failure patients (mean age 62.22  $\pm$  8.62 years, 69 men) was assessed through comprehensive cardiological and periodontal examinations. Patients were categorized into heart failure with reduced ejection fraction, mildly reduced ejection fraction, and preserved ejection fraction. Periodontal parameters, including probing pocket depth, clinical attachment loss, and bleeding on probing were evaluated. Microbiological and statistical analyses were conducted.

**Results.** Severe periodontitis (Stage C) was identified in 30% of patients, while 48% had moderate periodontitis (Stage B). Patients with chronic heart failure with reduced ejection fraction exhibited the highest prevalence of severe periodontitis, with a significant correlation between increased probing pocket depth and reduced ejection fraction. Candida species abundance was associated with lower ejection fraction ( $p < 0.0Y$ ) and advanced periodontitis ( $p < 0.0X$ ). Elevated NT-proBNP levels (1121.00–7611.00 pg/mL) correlated with Streptococcus mitis prevalence, while C-reactive protein levels (up to 2.35 mg/dL) were highest in patients with Klebsiella pneumoniae.

**Conclusion.** The study highlights a strong association between periodontal disease, microbial dysbiosis, and CHF. Findings suggest that oral microbial imbalances, particularly involving Candida, Streptococcus mitis, and Klebsiella pneumoniae, contribute to systemic inflammation and cardiovascular complications.

## Introduction

Chronic Heart Failure (CHF) is becoming a disease that is more common today.<sup>1</sup> As we look for surgical and preventive methods, this study analyzes the link between oral health and heart disease. Additional trials are needed to clarify further the causal relationship between the CHF and its cause. CHF is an inflammatory condition caused by bacteria in plaque, leading to the destruction of gum tissues and the bone of your jaws, and, if left untreated, can result in tooth loss.<sup>2</sup> Beyond the oral cavity, the inflammatory component of gum disease has been associated with

an increased risk of heart disease.<sup>2,3,4</sup> Also we can assuredly say that periodontists can affect a human's immune system by weakening the inflammatory response of the body to trigger various inflammatory diseases such as heart diseases, diabetes, swelling in arteries and kidney failure.<sup>5,6</sup>

Significant associations between oral health status and a number of systemic diseases have been established, including, but not limited to, cardiovascular diseases, Alzheimer's disease and dementia, obesity, diabetes and metabolic disorders, rheumatoid arthritis, and several cancers.<sup>7,8,9</sup>

In order to understand the true cause of systemic diseases better we can also consider microbiological background. By studying bacteria and its morphology and pathogenicity we can understand how viruses, fungi and bacteria have an enormous impact on human body immune response and the role of microbiology in pathophysiology.

#### Material and methods

A cohort of 98 patients with chronic heart failure was examined, comprising 69 men, with a mean age of  $62.22 \pm 8.62$  years. All participants underwent comprehensive cardiological evaluations. Patients with CHF were stratified into three groups according to their phenotype: heart failure with reduced ejection fraction (HFrEF), heart failure with mildly reduced ejection fraction (HFmrEF), and heart failure with preserved ejection fraction (HFpEF).

All included patients underwent a complete periodontal and dental examination. The oral assessment encompassed periodontal parameters, including probing pocket depth (PPD), clinical attachment loss (CAL), bleeding on probing (BOP), percentage of current bone loss, and diagnosis (stage). The periodontal screening index was employed to quantify the severity of periodontal disease. Attachment loss was calculated using probing depths and gingival recession measurements.

For microbiological assessment, microorganisms were initially cultured on nutrient media Endo agar, salt egg yolk agar, blood agar 5%, Sabouraud Agar and subsequently identified using the MALDI-TOF MS method.

**Ethical approval.** This study is based on de-identified and anonymous, aggregated healthcare data and does not involve direct patient interactions or their personal information. Ethical approval (2023/01-009) was obtained from institutional review board and all the analyses were conducted in compliance with national data protection regulations.

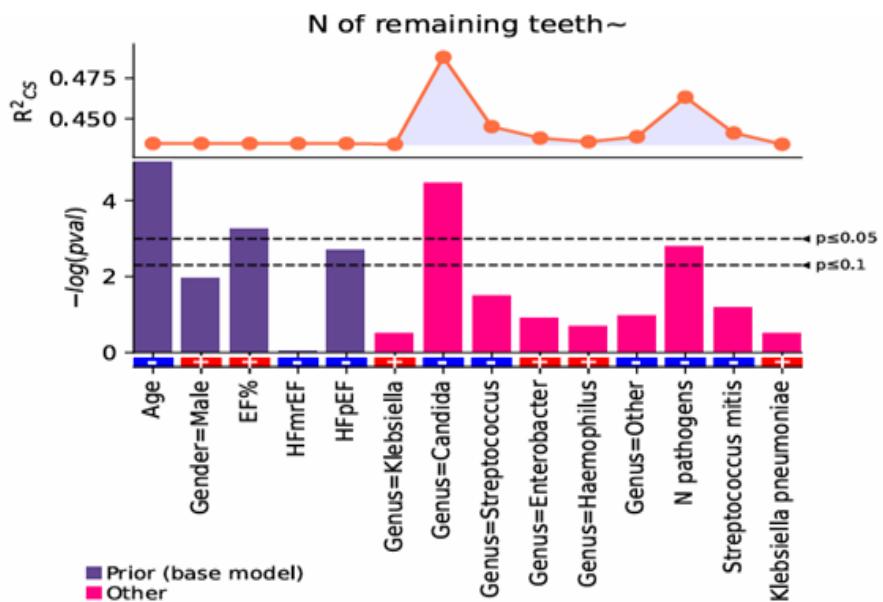
**Statistical analysis.** The statistical analysis included descriptive and analytical statistics where for variables with a normal distribution, parametric statistical methods were used and presented as means  $\pm$  standard deviation. Numerical variables of non-normally distributed data were presented as mean values  $\pm$  standard deviation. For all types of analysis, statistical significance was determined using the Student's t-test, with a significance level set at  $p < 0.05$ . Statistical analysis was performed using Python v3.9.16 and R v4.2.2. The Mann-Whitney U test and logistic regression were employed, accounting for age, sex, and various oral health parameters in relation to overall survival and cardiac events/transmissions. Data visualization was conducted with Matplotlib and Seaborn libraries.

#### Results

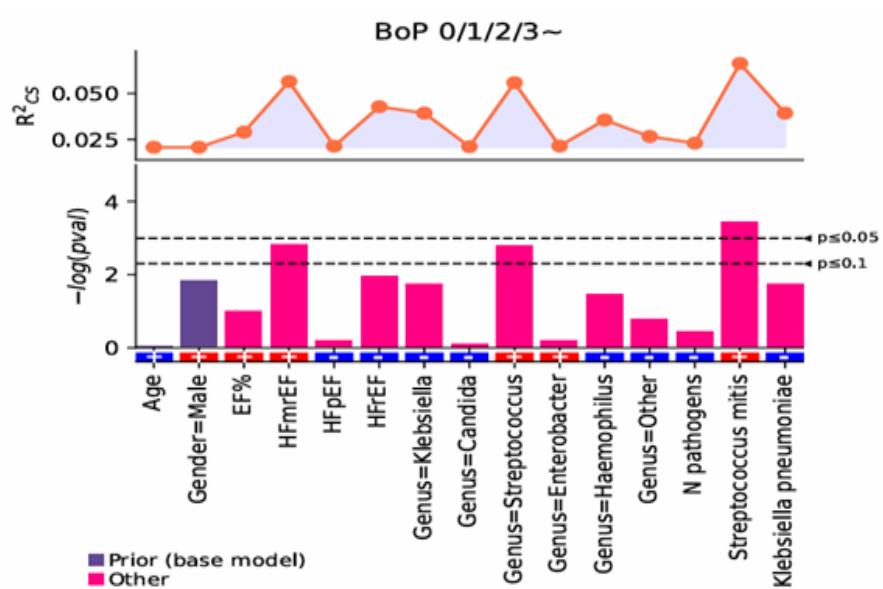
In this cohort study, severe periodontitis (Stage C) was observed in 59 (30%) patients, while moderate periodontitis (Stage B) was present in 94 (48%) patients. A higher prevalence of severe periodontitis was noted among patients with chronic heart failure with reduced ejection fraction (HFrEF). The investigation revealed a direct correlation between the greatest probing pocket depth (PPD) and both heart failure with mildly reduced ejection fraction (HFmrEF) and reduced ejection fraction (HFrEF), as depicted in Figure 1-6.

**Figure 1. Number of Remaining Teeth and Pathogen Load.**

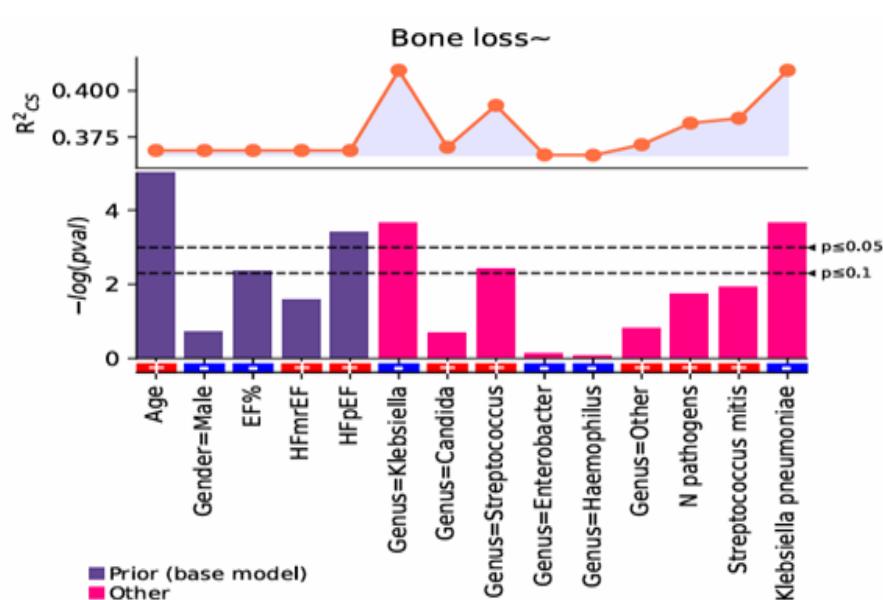
Inverse correlation between teeth count and pathogen abundance (*Streptococcus mitis*, *Klebsiella pneumoniae*), with adjustments for EF% and HF phenotypes ( $p < 0.05$ ).

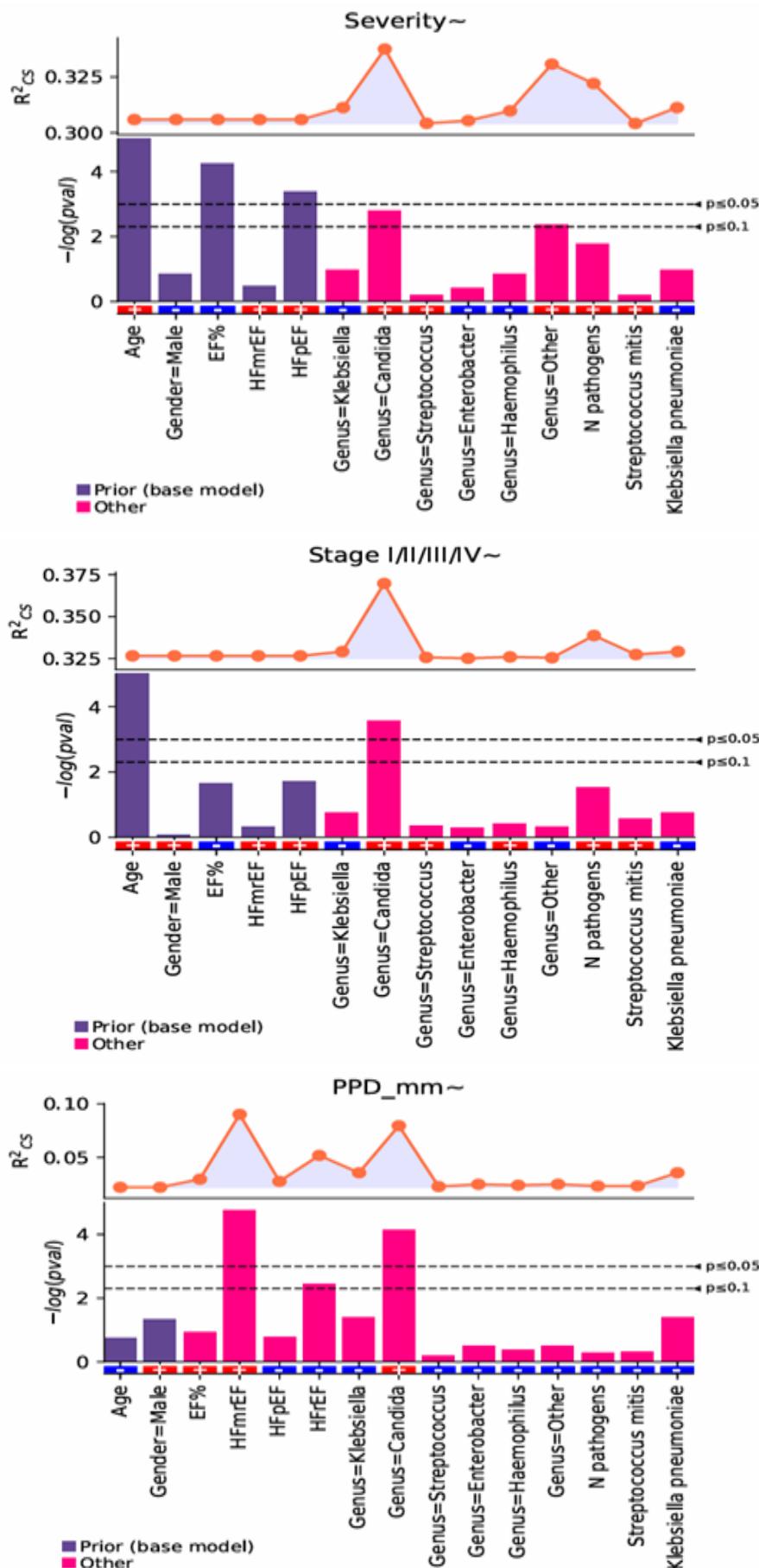
**Figure 2. Bleeding on Probing (BoP) Scores and Microbial Factors.**

BoP scores (0–3) linked to specific genera (*Candida*, *Streptococcus*) and HF phenotypes. Significant associations ( $p < 0.05$ ) highlighted.

**Figure 3. Alveolar Bone Loss and Cardiac-Microbial Interactions.**

Bone loss severity associated with *Klebsiella* and *Streptococcus* prevalence, stratified by HFmrEF/HFpEF. Polarization reflects effect size ( $\log(p\text{-value})$ ).




**Figure 4. Periodontal Severity and Microbial Dysbiosis.**

Relationship between periodontal severity ( $R^2 = 0.325-0.300$ ) and microbial genera (Klebsiella, Candida), adjusted for age, sex, and HF phenotypes.

**Figure 5. Periodontitis Stage (I-IV) and Systemic Predictors.**

Regression analysis of periodontitis stages (I-IV) against clinical variables (age, EF%, HF phenotypes) and microbial genera. Positive/Negative coefficients reflect directional associations ( $p < 0.1$ ).

**Figure 6. Probing Pocket Depth (PPD) by CHF Phenotype and Microbial Genera.**

Association between mean PPD (mm) and heart failure phenotypes (HFmrEF, HFmrEF, HFpEF), stratified by dominant oral microbial genera (Klebsiella, Candida, Streptococcus). Dashed line indicates significance ( $p < 0.05$ ).

Moreover, patients exhibiting a higher abundance of *Candida* species in their oral microbiome demonstrated significantly lower ejection fraction (EF) ( $p<0.0Y$ ), more advanced stages of periodontitis ( $p<0.0X$ ), and a reduced number of remaining teeth. It is postulated that *Candida* may exert direct influence on multiple factors potentially exacerbating heart failure progression. A significant association was observed between increased alveolar bone loss and extra-cardiac bacterial infections ( $p<0.05$ ).

Elevated NT-proBNP levels, ranging from 1121.00 to 7611.00 pg/mL, were detected in patients with a predominance of *Streptococcus mitis* in their oral microbiota. C-reactive protein levels ranged from 1.32 mg/dL to 1.51 mg/dL, with the highest level of 2.35 mg/dL associated with the presence of *Klebsiella pneumoniae* in the microbiota [4]. Notably, *Klebsiella* species, particularly *Klebsiella pneumoniae*, exhibited the highest prevalence among the microbial factors examined. The most significant PPD was associated with HFmrEF ( $p<0.08$ ).

As illustrated in Figures A, E, and F, a strong correlation was observed between *Candida* species and periodontal parameters, including the number of remaining teeth, probing pocket depth (PPD) ( $p<0.05$ ), and the stage of periodontitis. These findings suggest a complex interplay between oral microbial ecology, periodontal health, and cardiac function in patients with chronic heart failure.

### Discussion

This study investigated the association between periodontal status, systemic inflammation, and their impact on heart diseases. Our findings reveal a significant correlation between baseline periodontal status and microbial dysbiosis, particularly influenced by *Candida* species, *Streptococcus mitis*, and *Klebsiella pneumoniae*.<sup>7-9</sup>

We observed that severe periodontitis was more prevalent among patients with heart failure with reduced ejection fraction (HFrEF), with a direct correlation between the greatest probing pocket depth (PPD) and HFrEF. The most significant PPD was associated with heart failure with mildly reduced ejection fraction (HFmrEF).

Microbiological analysis revealed that a higher presence of *Candida* species was associated with significantly lower ejection fraction (EF), more advanced periodontitis stages, and fewer remaining teeth. *Streptococcus mitis* predominance correlated with elevated NT-proBNP levels, while *Klebsiella pneumoniae* presence was linked to the highest levels of C-reactive protein.

Our results align with previous research suggesting that improved oral hygiene may contribute to a reduction in heart failure incidence. *Youn Huh et al.* reported that daily tooth brushing is associated with decreased heart failure rates.<sup>2</sup> *Rebecca L. Molinsky et al.* noted that heart failure remains a significant health concern for over a decade and is directly related to periodontal status. U.S. national data samples further support the association between heart failure and periodontitis.<sup>3</sup>

Notably, *Syed Adeel Hassan et al.* reported that *Klebsiella pneumoniae*, accounting for 5% of cases, is responsible for mortality in aortic and mitral valve conditions in nearly all instances.<sup>7</sup>

While our study did not explicitly examine differences in microbiological characteristics for heart failure with preserved ejection fraction (HFpEF), the findings suggest variations across different heart failure phenotypes. These results underscore the complex relationship between oral health, microbial ecology, and cardiovascular outcomes, highlighting the potential importance of periodontal care in managing heart failure risk.

Data indicate that in patients with CHF, 48% of patients with chronic heart failure have moderate periodontitis and 30% have severe periodontitis. This is generally consistent with the published literature. For example, *Schulze-Späte et al.* found that 69% of patients with heart failure had moderate to severe periodontitis.<sup>10</sup> However, exact percent-

ages may vary between studies due to differences in classification criteria and patient populations.

The mention of *Candida*, *Streptococcus mitis* and *Klebsiella pneumoniae* contributing to systemic inflammation is consistent with current research. Review by *Liccando et al.* discusses how oral pathogens may contribute to systemic inflammation and cardiovascular disease.<sup>11</sup> However, the specific bacteria mentioned may vary between studies because the oral microbiome is complex and diverse.

CRP is a widely accepted marker of systemic inflammation. Numerous studies have shown a positive correlation between periodontal disease and elevated CRP levels. Meta-analysis by *Shailly Luthra et al.* found that patients with periodontitis had significantly higher levels of CRP compared to controls.<sup>12</sup> *Gomez-Filho et al* reported that severe periodontitis was associated with higher CRP levels, even after adjusting for other cardiovascular risk factors.<sup>13</sup> Some studies have looked at multiple inflammatory markers simultaneously. *Madeline X F Kosho et al.* found that patients with generalized periodontitis had significantly higher levels of CRP, IL-6, and neutrophils compared with controls.<sup>14</sup> A study by *Neeraj Gugnani et al.* showed that intensive periodontal treatment resulted in improved endothelial function and decreased levels of several inflammatory markers, including CRP and IL-6.<sup>15</sup>

It is important to note that although these associations are consistently observed, the relationships are complex and likely bidirectional. Periodontal disease can contribute to systemic inflammation, but systemic inflammation can also affect periodontal health. Moreover, the precise mechanisms linking periodontal disease to elevated inflammatory markers are still being elucidated. We propose several pathways: translocation of oral bacteria into the bloodstream; systemic distribution of inflammatory mediators from periodontal tissues; and immune response to periodontal pathogens affecting distant sites.

Although the association between periodontal disease and inflammatory markers is well established, more research is needed to fully understand the cause-and-effect relationships and potential implications for cardiovascular health.

**Limitations.** The study examined 98 patients, which may limit the generalizability of the findings to larger populations. The study doesn't mention a control group of individuals without heart failure, which could have provided a baseline for comparison. While the study accounted for age and sex, there might be other unmeasured confounding factors influencing the relationship between periodontal disease and heart failure. Without follow-up data, the study cannot assess how changes in periodontal status might affect heart failure progression over time.

**What's known?** Periodontitis has been linked to various systemic diseases, including cardiovascular conditions such as CHF. Studies suggest that bacterial infections in the oral cavity can contribute to systemic inflammation, which may lead to heart disease. Research has identified inflammatory markers, such as CRP, as being elevated in patients with both periodontitis and cardiovascular disease. Additionally, previous studies indicate that poor oral hygiene and microbial dysbiosis play a role in increasing the risk of CHF by weakening the immune system and promoting inflammatory responses that contribute to endothelial dysfunction and cardiac stress.

**What's new?** This study highlights a direct association between periodontitis severity and CHF phenotypes, demonstrating that severe periodontitis is more prevalent among patients with heart failure with HFrEF. A significant correlation was found between advanced periodontal disease markers, such as PPD, and lower ejection fraction levels. The findings also introduce the role of specific microbial species, including *Candida*, *Streptococcus mitis*, and *Klebsiella pneumoniae*, in exacerbating CHF progression. The study suggests

that microbial dysbiosis in the oral cavity may contribute to systemic inflammation and CHF-related complications, emphasizing the need for periodontal care in CHF management.

### Conclusion

This study reveals a significant association between periodontal disease, microbial dysbiosis, and chronic heart failure. The complex interplay between oral health and cardiac function underscores the potential importance of periodontal care in managing heart failure risk. Further research is warranted to elucidate causal relationships and develop targeted interventions.

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**Authors' Contributions:** Concept and design of the study, control of the research, approval of the final version of the article: M.B., A.S., A.K.; Collection and preparation of data, primary processing of the material and their verification: B.A., D.Y.; performance of the statistical analysis: A.T., B.A., S.J.; Writing the text of the article (introduction, discussion, conclusion): N.K., A.Z., I.L. Writing the text of the article (methods, results): B.A., A.T., N.K. All authors reviewed, edited, and approved the final version of the manuscript.

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