Oral Lesions in HIV-Positive Patients: A Retrospective Study from a Histopathology Service

Lesões Orais em pacientes HIV+: Estudo Retrospectivo em um Serviço de Histopatologia

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Abstract

Aim: HIV-associated oral lesions may serve as predictive indicators of immunosuppression, assisting in both the diagnosis and monitoring of disease progression in affected patients. Therefore, this study aimed to retrospectively analyse biopsied HIV-associated oral lesions diagnosed by a specialised histopathology service, with emphasis on patient and lesion characteristics. Materials and methods: A retrospective cross-sectional study was conducted to analyse cases of HIV-associated oral lesions from the DCOD, covering records from January 1981 to December 2024. Results: Among the 26,947 reports analysed, 83 were suggestive of HIV-associated lesions, of which 24 patients had confirmed infection. Kaposi sarcoma and non-Hodgkin lymphoma were the most frequent diagnoses. Most patients were male (75%), with a mean age of 46 years (SD = 14.91). Conclusion: This retrospective study met its objectives by characterising the demographic profile of affected patients and describing the clinical features of HIV-associated oral lesions diagnosed at a regional referral centre.

Keywords: HIV Infections; Oral Medicine; Oral Manifestations.

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Introduction

Human Immunodeficiency Virus (HIV) infection leads to progressive immunosuppression through the depletion of CD4+ T lymphocytes, increasing vulnerability to opportunistic infections and neoplastic conditions.[1,2] Oral manifestations are common in this context, affecting 20% to 50% of individuals living with HIV.[3]

Kaposi sarcoma (KS), non-Hodgkin lymphoma (NHL), oral candidiasis, periodontal disease, and hairy leucoplakia are strongly linked to the infection.[4] These oral lesions may serve as predictive indicators of immunosuppression, assisting both in diagnosis and in the monitoring of disease progression in affected patients.[5]

Although global HIV incidence and mortality have declined over the past decade, the disease remains a major public health concern.[6] In 2023, an estimated 39.9 million people were living with HIV worldwide, with more than 1.3 million new infections reported; Brazil alone registered 46,495 new cases.[1,7] Despite the benefits of antiretroviral therapy, which has substantially reduced the occurrence of HIV-related oral lesions, such conditions continue to present clinically significant diagnostic value.[8]

In Southern Brazil, a key service for the clinical and histopathological diagnosis of oral diseases is the Diagnostic Centre for Oral Diseases (DCOD) of the School of Dentistry, Federal University of Pelotas (RS, Brazil), which serves as a regional reference. Recognising that oral manifestations of HIV infection are not uncommon and can hold significant diagnostic value for the disease, often leading to the identification of the infection itself, this study aimed to conduct a retrospective survey of biopsied HIV-associated oral manifestation cases diagnosed by the DCOD. The study sought to characterise the demographic profile of affected patients and the clinical features of the lesions, to provide an updated overview of their frequency, demographic distribution,

and clinical presentation. This analytical approach aimed to expand regional epidemiological understanding and enhance diagnostic awareness.

Materials and Methods

Study Design and Ethical Considerations

A retrospective cross-sectional study was conducted to analyse cases of HIV-associated oral lesions from the DCOD, covering records from January 1981 to December 2024. The study adhered to the guidelines for Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).[9] It was approved by the Ethics Committee of the Federal University of Pelotas (No. 74484023.1.0000.5317) and conducted in accordance with the Declaration of Helsinki.

Sample

The sample comprised cases of HIV-associated oral lesions that underwent biopsy in confirmed HIV-positive patients, diagnosed by the DCOD between January 1981 and December 2024. Lesions were classified according to the EC Clearinghouses and World Health Organization criteria (1993).[4] Cases were excluded if clinical and demographic data were insufficient for comprehensive collection, or if the HIV diagnosis could not be corroborated through medical records or by the Specialised HIV/AIDS Care Service (SAE) at the UFPel Medical School outpatient clinic.

Data Collection

Cases exhibiting a histopathological diagnosis of oral manifestations consistent with the scope of the study were selected. All histological slides were reviewed by an experienced oral pathologist to ensure accurate inclusion in the study. Subsequently,

clinical records were analysed to confirm HIV infection, based on patient self-report or on laboratory tests requested by the DCOD for suspected cases. For patients external to the DCOD service, an active search was conducted within the SAE records to confirm their registration within the HIV patient database.

An Excel® spreadsheet (Microsoft Windows, Redmond, Washington, USA) was created. For all cases meeting the inclusion criteria, the following data were collected when available: diagnosis of the oral manifestations; year of oral diagnosis; sex (male or female); age (years); anatomical location (hard palate, soft palate, buccal mucosa, lip, tongue, floor of mouth, gingiva, maxilla, and mandible); fundamental lesion (papule, nodule, bulla, vesicle, ulcer, erosion, or macule); previous diagnosis of HIV infection (presence/absence); and treatment for HIV infection (presence/absence).

Statistical Analysis

Descriptive statistical analysis of the data was performed using frequency, mean, standard deviation, and range for quantitative variables, and frequency for qualitative variables. Analyses were performed using Microsoft Excel 365 (Microsoft Windows, Redmond, Washington, USA).

Results

From January 1981 to December 2024, the DCOD processed 26,947 histopathological reports. Of these, 83 (0.30%) corresponded to oral lesions potentially associated with HIV. Among these, HIV seropositivity was confirmed in 24 patients (0.08%). (Table 1)

Table 1. Demographic and clinical characteristics of HIV-positive patients diagnosed with HIV-associated oral lesions at the DCOD between 1981 and 2024.

Variable	n (%)
Oral lesions associated to HIV identified in HIV-positive patients (n=24)	
Kaposi Sarcoma	7 (29.17)
Non-Hodgkin lymphoma	7 (29.17)
Histoplasmosis	6 (25.00)
Condyloma Acuminatum	3 (12.50)
Tuberculosis	1 (4.16)
Sex distribution (n=24)	
Male	18 (75.00)
Female	6 (25.00)
Age distribution (n=24)	
Mean age	46±14.91 years
Age range	26-80 years
Prior HIV diagnosis at the time of biopsy (n=24)	
Presence	18 (75.00)
Absence	6 (25.00)
Antiretroviral therapy status at time of biopsy* (n=18)	
Current antiretroviral therapy	9 (50.00)
Discontinued antiretroviral therapy	2 (11.11)
Antiretroviral therapy status unknown	7 (38.88)

*Data from patients with a prior HIV diagnosis.

Oral candidiasis and oral hairy leukoplakia, both strongly associated with HIV, occurred in patients whose seropositivity could not be confirmed.

A higher concentration of cases was observed in the fourth (n = 6; 26.08%) and fifth decades of life (n = 8; 34.78%). Cases occurred between 1994 and 2024, with a predominance (54%) observed during the period from 2014 to 2024.

Among the seven reported cases of KS, six (85.71%) occurred in men and one (14.28%) in a woman. Clinically, the disease consistently presented as nodules, primarily located on the hard palate (n = 6; 85.71%) or buccal mucosa (n = 1; 14.28%). In two (28.57%) of these cases, an associated macule was also observed.

NHL accounted for seven cases, with four (57.14%) occurring in women and three (42.85%) in men. The lesions manifested as nodules on the hard palate (n = 5; 72.42%) or buccal mucosa (n = 2; 28.57%).

Histoplasmosis represented six cases, comprising five (83.33%) in men and one (16.66%) in a woman. Clinically, the disease presented as nodules (n = 4; 66.66%) or ulcers (n = 2; 33.33%), located on the tongue (n = 2; 33.33%), hard palate (n = 2; 33.33%), both tongue and hard palate (n = 1; 16.66%), or the buccal mucosa (n = 1; 16.66%). (Figure 1)

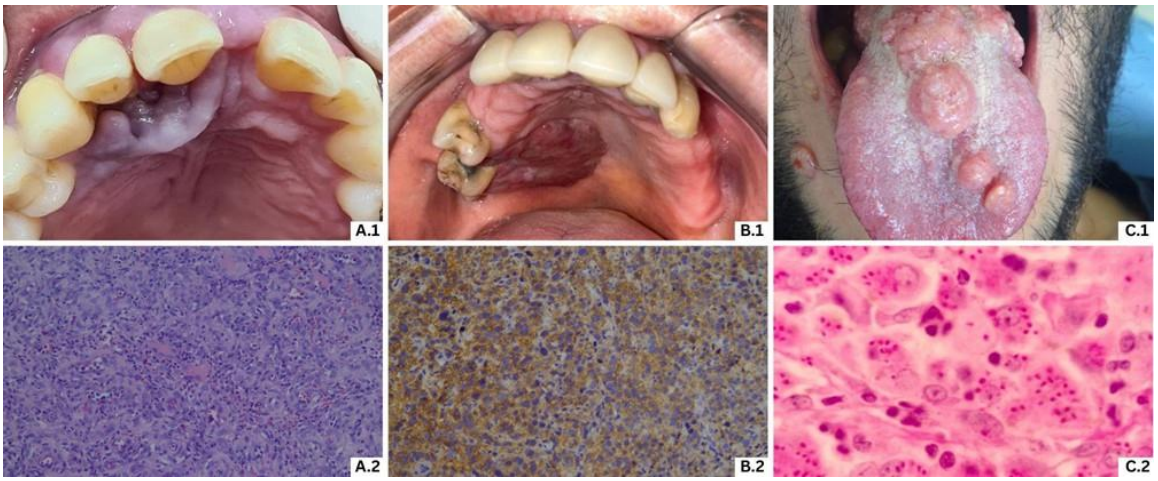

Figure. 1 Clinical and histopathological features of oral lesions associated with HIV in HIV positive patients. A) Oral Kaposi Sarcoma. A.1) Submucosal nodule with an irregular surface and purplish colouration extending across the anterior palate and into the region of the anterior teeth and premolars. A.2) Presence of fibrous connective tissue stroma with numerous irregular slit-like spaces containing extravasated red blood cells, surrounded by ill-defined fascicles of spindle-shaped cells (Haematoxylin

and eosin stain, 200x). B) Oral Non-Hodgkin Lymphoma B.1) Nodule with an irregular surface and reddish colouration, located on the hard palate in the region of the right molars. b.2) Oral plasmablastic lymphoma showing neoplastic cells expressed a plasma cell phenotype, being positive for CD138 (immunohistochemistry, 200x). C) Histoplasmosis. C.1) Multiple superficial, irregular, pink nodules on the dorsal surface of the tongue. C.2) Histoplasmosis presenting numerous fungal elements (yeast of *H. capsulatum)* reactive to Periodic acid-Schiff (400x*).*

The three cases of condyloma acuminatum all occurred in men with a pre-existing diagnosis of HIV infection. The lesions consistently presented as nodules (100%) on the buccal mucosa (n = 2; 66.66%) and lips (n = 1; 33.33%).

A single case of tuberculosis was collected from a male patient with a prior diagnosis of HIV infection, who was undergoing antiretroviral treatment. His lesion clinically presented as an ulcer on the tongue.

Discussion

One-quarter of the patients in this study received their HIV diagnosis only after presenting with an oral lesion, underscoring the critical role of oral health services in the detection of the infection. This finding reinforces that, despite advances in screening and widespread availability of testing, oral manifestations remain an important clinical gateway to diagnosis, particularly in settings where individuals may have limited access to routine medical care.

A systematic review revealed that oral candidiasis has consistently remained the most prevalent oral manifestation among individuals living with HIV.[10] Despite its high prevalence, oral candidiasis is rarely subjected to biopsy, which explains its absence

from the present study sample. This limitation also applies to periodontal diseases, which are strongly associated with HIV-positive individuals and are frequently reported in other case series.[11-15]

Clinical studies indicate that among the HIV-associated lesions commonly submitted for biopsy, KS is the most prevalent manifestation.[3,13,14,16-22] These findings are consistent with the results of the present study, in which KS was the most frequently diagnosed lesion, accompanied by NHL. Although the absolute number of cases is small relative to the total number of diagnoses made by the service, this frequency may reflect the significant decline in the incidence of these neoplasms following the introduction of ART.[23]

NHL is one of the primary malignancies associated with HIV infection, with seropositive individuals presenting a 23-fold increased risk of developing the disease compared with the general population.[24]

The oral cavity is an uncommon site for the development of NHL, accounting for only 2% of all extranodal lymphomas.[25] The occurrence of oral NHL among people living with HIV is absent from numerous clinical surveys, including Brazilian studies.[3,13,14,16-19,22,26] However, when specifically considering HIV-associated oral lesions most frequently submitted for biopsy, NHL emerges as the second most prevalent malignancy.[14,20,21,27]

Regarding anatomical distribution, the majority of NHL cases in the present study were located on the hard palate, a pattern consistent with the findings of a Brazilian multicentre study.[28]

Histoplasmosis is a highly endemic infection in Brazil and represents the most clinically significant endemic mycosis in Latin America, particularly among people living with HIV, in whom it frequently manifests at extrapulmonary sites.[29-31] Oral lesions of disseminated histoplasmosis show a predilection for the tongue, palate, and buccal

mucosa. In general, patients present with painful ulcers that may persist for several weeks.[32] These findings are consistent with the clinical characteristics observed in the present study.

HIV-associated immunosuppression complicates the control of human papillomavirus (HPV) infections.[33] Studies suggest that oral manifestations of HPV continue to evolve in the era of ART.[33-36] It has been hypothesised that this increased risk is a consequence of extended patient survival in the post-ART era; prior to the availability of ART, HIV-infected individuals often progressed to AIDS and died before HPV-associated lesions could become clinically apparent.[33] A notable limitation of the present study, however, is the unavailability of information regarding ART use among patients diagnosed with condyloma acuminatum.

Although the literature indicates a reduction in the prevalence of HIV-associated oral lesions over recent decades, the present study observed an increase in the number of cases diagnosed by the service. This rise may not reflect a true increase in lesion incidence, but rather a greater demand for specialised diagnostic services, coupled with improved access to healthcare and enhanced clinical recognition of these manifestations by professionals. Additionally, the more open discourse surrounding HIV in recent decades may have contributed to reduced stigma and, consequently, to higher rates of notification and referral of suspected cases.

Conclusion

This retrospective study met its objectives by characterising the demographic profile of affected patients and describing the clinical features of HIV-associated oral lesions diagnosed at a regional referral centre. The findings reinforce the ongoing diagnostic relevance of these manifestations, particularly given that a substantial

proportion of patients received their HIV diagnosis only after presenting with an oral lesion. Additionally, the observed increase in identified cases in recent years, despite broader epidemiological trends indicating a decline in the prevalence of such lesions, likely reflects improved access to specialised diagnostic services and greater clinical awareness among healthcare professionals. Together, these observations underscore the importance of oral healthcare settings as key points for early detection, clinical monitoring, and integration with broader HIV care pathways.

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Resumo

Objetivo: As lesões orais associadas ao HIV podem atuar como indicadores preditivos de imunossupressão, auxiliando tanto no diagnóstico quanto no monitoramento da progressão da doença em pacientes acometidos. Dessa forma, este estudo teve como objetivo analisar retrospectivamente lesões orais associadas ao HIV submetidas à biópsia e diagnosticadas por um serviço especializado em histopatologia, com ênfase nas características dos pacientes e das lesões. Materiais e métodos: Foi realizado um estudo retrospectivo de corte transversal para analisar casos de lesões orais associadas ao HIV provenientes do CDDB, abrangendo registros de janeiro de 1981 a dezembro de 2024. Resultados: Entre os 26.947 laudos analisados, 83 foram sugestivos de lesões associadas ao HIV, dos quais 24 pacientes tiveram a infecção confirmada. Sarcoma de Kaposi e linfoma não Hodgkin foram os diagnósticos mais frequentes. A maioria dos pacientes era do sexo masculino (75%), com média de idade de 46 anos (DP = 14,91). Conclusão: Este estudo retrospectivo atingiu seus objetivos ao caracterizar o perfil demográfico dos pacientes acometidos e descrever as características clínicas das lesões orais associadas ao HIV diagnosticadas em um centro de referência regional.

References

1. World Health Organization. HIV/AIDS: fact sheet. 2023. Available at https://www.who.int/news-room/fact-sheets/detail/hiv-aids (accessed April 2025).

2. Le Hingrat Q, Sereti I, Landay AL, Pandrea I, Apetrei C. The Hitchhiker Guide to CD4+ T-Cell depletion in lentiviral infection. A critical review of the dynamics of the CD4+ T Cells in SIV and HIV infection. Front Immunol 2021; 12:695674.

3. Mwangosi IEAT, Tillya J. Oral lesions associated with HIV/AIDS in HIV-seropositive patients attending a counselling and treatment centre in Dar es Salaam. Int Dent J. 2012; 62(4):197-202.

4. EC-Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of the Immunodeficiency Virus. Classification and diagnostic criteria for oral lesions in HIV infection. J Oral Pathol Med. 1993; 22(7):289-91.

5. Indrastiti RK, Wardhany II, Soegyanto AI. Oral manifestations of HIV: Can they be an indicator of disease severity? (A systematic review). Oral Dis. 2020; 26(Suppl. 1):133-136.

6. UNAIDS. Global HIV & AIDS statistics — Fact sheet. 2024. Available at: https://www.unaids.org/en/resources/fact-sheet (accessed April 2025).

7. Brazilian Ministry of Health - Department of HIV/AIDS, Tuberculosis, Viral Hepatitis and Sexually Transmitted Infections. Epidemiological Bulletin HIV and AIDS 2024. Ministry of Health; 2024.

8. Hodgson TA, Greenspan D, Greenspan JS. Oral lesions of HIV disease and HAART in industrialized countries. Adv Dent Res. 2006; 19(1):57-62.

9. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008; 61:344-9.

10. El Howati A, Tappuni A. Systematic review of the changing pattern of the oral manifestations of HIV. J Invest Clin Dent. 2018; 9:e12351.

11. Chen Y, Li A, Yang Y, Lu J, Xu Y, Ji X, et al. Global, regional and national burden of HIV/AIDS among individuals aged 15-79 from 1990 to 2021. AIDS Res Ther. 2025; 22(1):51.

12. Arendorf TM, Bredekamp B, Cloete CAC, Sauer G. Oral manifestations of HIV infection in 600 South African patients. J Oral Pathol Med. 1998; 27(4):176-9.

13. Fabian FM, Kahabuka FK, Petersen PE, Shubi FM, Jürgensen N. Oral manifestations among people living with HIV/AIDS in Tanzania. Int Dent J. 2009; 59(4):187-91.

14. Berberi A, Noujeim Z. Epidemiology and relationships between CD4+ counts and oral lesions among 50 patients infected with human immunodeficiency virus. J Int Oral Health. 2015; 7(1):18-21.

15. Souza BKL, Faé DS, Lemos CAA, Verner FS, Machado RA, Ortega RM, Aquino SN. Associated oral manifestations with HIV southeastern Brazilian patients on antiretroviral therapy. Braz J Otorhinolaryngol. 2023; 89:425-31.

16. Moniaci D, Greco D, Flecchia G, Raiteri R, Sinicco A. Epidemiology, clinical features and prognostic value of HIV-1 related oral lesions. J Oral Pathol Med. 1990; 19:477-81.

17. Eyeson JD, Tenant-Flowers M, Cooper DJ, Johnson NW, Warnakulasuriya KAAS. Oral manifestations of an HIV positive cohort in the era of highly active anti-retroviral therapy (HAART) in South London. J Oral Pathol Med. 2002; 31(3):169-74.

18. Ramírez-Amador V, Esquivel-Pedraza L, Sierra-Madero J, Anaya-Saavedra G, González-Ramírez I, Ponce-de-León S. The changing clinical spectrum of human immunodeficiency virus (HIV)-related oral lesions in 1,000 consecutive patients: a 12-year study in a referral center in Mexico. Medicine (Baltimore). 2003; 82(1):39-50.

19. Pinheiro A, Marcenes W, Zakrzewska JM, Robinson PG. Dental and oral lesions in HIV infected patients: a study in Brazil. Int Dent J. 2004; 54(3):131-7.

20. Tirwomwe JF, Rwenyonyi CM, Muwazi LM, Besigye B, Mboli F. Oral manifestations of HIV/AIDS in clients attending TASO clinics in Uganda. Clin Oral Invest. 2007; 11:289-92.

21. Lourenço AG, Motta ACF, Figueiredo LTM, Machado AA, Komesu MC. Oral lesions associated with HIV infection before and during the antiretroviral therapy era in Ribeirão Preto, Brazil. J Oral Sci. 2011; 53(3):379-85.

22. Bartholo MF, Tenório JR, Andrade NS, Shibutani PP, Martins F, Gallottini M. Orofacial manifestations in Brazilian people living with HIV/AIDS under long-term antiretroviral therapy: a cross-sectional study. Oral Surg Oral Med Oral Pathol Oral Radiol. 2023; 136(4):436-441.

23. Borges ÁH. Combination antiretroviral therapy and cancer risk. Curr Opin HIV AIDS. 2017; 12(1):12-9.

24. Chen Y, Zhao J, Sun P, Cheng M, Xiong Y, Sun Z, et al. Estimates of the global burden of non-Hodgkin lymphoma attributable to HIV: a population attributable modeling study. eClinicalMedicine. 2024; 67:102370.

25. Barone S, Buffone C, Ferrillo M, Pasqua F, Parrotta S, Salviati M, et al. Oral malignant non-Hodgkin lymphoma: A retrospective single-center study. Int J Environ Res Public Health. 2022; 19(5):2605.

26. Ceballos-Salobrena A, Gaitan-Cepeda LA, Ceballos-Garcia L, Lezama-Del Valle D. Oral lesions in HIV/AIDS patients undergoing highly active antiretroviral treatment including protease inhibitors: A new face of oral AIDS? AIDS Patient Care STDs. 2000; 14(12):627-35.

27. Zhang X, Reichart PA, Song Y. Oral manifestations of HIV/AIDS in China: a review. Oral Maxillofac Surg. 2009; 13(1):63–8.

28. De Arruda JAA, Schuch LF, Neto NC, de Souza LL, Rodrigues-Fernandes CI, Abreu LG, et al. Oral and oropharyngeal lymphomas: a multi-institutional collaborative study. J Oral Pathol Med. 2021; 50(7):717-26.

29. Gómez B L. Histoplasmosis: Epidemiology in Latin America. Curr Fungal Infect Rep. 2011; 5(4):199-205.

30. Cano-Torres J O, Olmedo-Reneaum A, Esquivel-Sánchez J M, Camiro-Zuñiga A, Pérez-Carrisoza A, Madrigal-Iberri C, et al. Progressive disseminated histoplasmosis in Latin America and the Caribbean in people receiving highly active antiretroviral therapy for HIV infection: A systematic review. Med Mycol. 2019; 0:1-9.

31. Falci D R, Dalla Lana D F, Pasqualotto A C. The era of histoplasmosis in Brazilian endemic mycoses. Lancet Reg Health Am. 2021; 3:100037.

32. Folk GA, Nelson BL. Oral Histoplasmosis. Head Neck Pathol. 2017; 11(4):513-6.

33. Ceccarelli M, Rullo E V, Facciolà A, Madeddu G, Cacopardo B, Taibi R, et al. Head and neck squamous cell carcinoma and its correlation with human papillomavirus in people living with HIV: a systematic review. Oncotarget. 2018; 9(24):17171-80.

34. Greenspan D, Canchola AJ, MacPhail LA, Cheikh B, Greenspan JS. Effect of highly active antiretroviral therapy on frequency of oral warts. Lancet. 2001; 357(9266):1411–2.

35. King MD, Reznik DA, O'Daniels CM, Larsen NM, Osterholt D, Blumberg HM. Human Papillomavirus-Associated Oral Warts among Human Immunodeficiency Virus-Seropositive Patients in the Era of Highly Active Antiretroviral Therapy: An Emerging Infection. Clin Infect Dis. 2002; 34(5):641–8.

36. Baccaglini L, Atkinson JC, Patton LL, Glick M, Ficarra G, Peterson DE. Management of oral lesions in HIV-positive patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007; 103(suppl 1):S50.e1-S50.e23.

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