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Original Article

Clinical application of computed tomography in differential diagnosis of malignant and benign lesions in maxilla

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Abstract: Our aim was to identify the computed tomographic (CT) characteristics most useful to differentiate malignant maxillary tumors (MMTs) from benign maxillary lesions (BML). A retrospective review of CT findings was performed in patients with histopathologically confirmed, untreated maxillary lesions. Logistic regression analysis was performed to evaluate the associations between CT characteristics and malignancy. Patients were divided into three groups according to the summed scores of five CT characteristics. We identified 159 patients with MMT and 132 patients with BML. After multivariable analyses, patients with MMT remained more likely to have cortical destruction and soft tissue extension than those with BML (odds ratio [OR], 49.9, 95% confidence interval [CI], 4.4-560.5 and OR, 17.5, 95% CI, 6.9-44.3, respectively). Compared with a summed CT score of < 2, patients with a score of 2-4 and ≥ 4 were 20 and 430 times more likely to have MMT (OR, 20.1, 95% CI, 4.3-94.7 and OR, 430.5, 95% CI, 87.6-2015.7, respectively). CT provides valuable information about differentiating malignant and benign maxillary lesions, particularly the presence of cortical involvement and soft tissue extension. The value of multi-parametric CT may highly increase such a differential diagnosis. Larger studies are needed to validate our findings.

Keywords: Computed tomography, maxilla, malignancy, differential diagnosis, benign

Introduction

A wide range of pathological conditions, both benign and malignant, affect the maxilla [1, 2]. Some lesions are discovered on routine dental X-rays, whereas others are found during examinations of the oral cavity and teeth. An accurate differential diagnosis is important for planning the treatment and management of maxillary lesions but rarely possible if diagnosis is solely based on clinical findings and conventional radiographs, such as intraoral and occlusal radiographs and panoramic X-rays [3]. The precise radiological evaluation of lesions in the maxilla is relatively difficult due to the anatomical complexity of the area. Therefore, cross-sectional imaging such as computed tomography (CT) or magnetic resonance imaging (MRI) is usually essential to evaluate the characteristics of maxillary lesions. CT has been valuable and widely used in demonstrating the extent of disease in the maxilla because of its ability to visualize soft tissues as well as the adjacent bony landmarks.

However, the role of CT in the differential diagnosis of malignant maxillary tumors (MMTs) and benign maxillary lesions (BMLs) is not well established, and there are currently no criteria for differentiating MMT from BML on CT. Previous studies to compare the imaging presentation of benign and malignant maxillary masses were relatively small or evaluated highly selected patient populations [4-9], and there have been advances in diagnostic imaging since the reports were published. Accurate differential diagnosis in individual patients with maxillary lesions would allow clinicians to select the most appropriate treatment for each patient, leading to improved survival and better quality of life. Therefore, the purpose of the present study was to determine whether MMTs

have different CT characteristics than BMLs and to identify the CT characteristics most useful for making a differential diagnosis in patients with maxillary lesions.

Materials and methods

Study patients

We retrospectively reviewed the CT findings in patients with histopathologically confirmed, previously untreated maxillary lesions between January 1, 2001, and December 31, 2013. We recorded the following demographic and clinical characteristics: sex, age, smoking status, alcohol use, disease stage, treatment, and imaging characteristics (e.g., enhancement, lesion texture, margins, cortical integrity, soft tissue extension, and cervical lymphadenopathy). "Ever drinkers" were defined as patients who had drunk at least one alcoholic beverage per week for at least 1 year during their lifetime, and patients who had never had such a pattern of drinking were considered "never drinkers". Patients who had smoked at least 100 cigarettes in their lifetime were defined as "ever smokers", and patients who had smoked fewer than 100 cigarettes in their lifetime were categorized as "never smokers" [10]. Preoperative CT had been performed within 7 days before surgery and histopathological confirmation. Patients were excluded for any of the following reasons: (1) CT artifacts interfered the diagnosis; (2) previously diagnosed head and neck cancer; and (3) treatment of a head and neck lesion (surgical management or radiotherapy) before the CT examination. The institutional review board of Shanghai Ninth People's Hospital approved this retrospective study.

CT acquisition and imaging interpretation

All CT examinations had been performed on a 64-channel scanner system (Philips Brilliance; Philips Medical Systems, Best, The Netherlands). The scanning parameters were as follows: 200-300 mAs; 120-140 kV voltage; 23 cm field of view (FOV); 256×256 matrix size; and 5 mm slice thickness with 1-1.25 mm reconstructions. Contrast-enhanced CT scans had been performed using dual-phase CT with 30- and 60-second delays. For contrast, a dose of 1.5 mL/kg body weight of iopamidol (Iopamiro 320, Bracco, Milan, Italy) or iopromide (Ultravist 300, Schering, Germany) was intravenously administered with a power injector at a rate of 2.5 mL/s.

The retrospectively obtained CT images were interpreted in consensus by three radiologists (Y.Y., Y.W., and X.T.) with more than 8 years of experience in the interpretation of head and neck CT images. All reviewers were blinded to the surgical and histopathologic results. Each lesion was evaluated with regard to enhancement (enhanced or not enhanced), texture (homogeneous or heterogeneous based on plain and/or contrast-enhanced CT images), margins (well-defined [more than two thirds of the margin sharply defined] or ill-defined [less than one-third of the margin sharply defined] [11]), cortical integrity (cortical destruction and perforation or no cortical destruction and perforation), soft tissue involvement (extension into adjacent soft tissue [muscle, fat, or neurovascular structures] or no involvement of adjacent soft tissue), and cervical lymph nodes (lymphadenopathy was defined as a cervical lymph node with a minimal axial diameter larger than 10 mm or with visualized necrosis [12]). These properties of CT images of MMT and BML are shown in **Figure 1** (A: MMT and B: BML).

Statistical analysis

Statistical analysis was carried out using STATA version 10.0 (College Station, TX). $P < 0.05$ was considered statistically significant. Demographic, clinical, and imaging characteristics were compared between the patients with MMT and BML using χ^2 testing (the Fisher exact test was used where appropriate) for categorical variables and the unpaired *t* test for noncategorical data. Odds ratios (OR) with 95% confidence intervals (CI) were calculated using univariate and multivariable logistic regression models with adjustment for possible confounding factors to determine the association between maxillary malignancy and CT characteristics.

The combined effects of the CT characteristics on lesion discrimination were then calculated. Each CT characteristic was scored as a 0 for negative results or a 1 for positive results as follows: inner texture (heterogeneous, 1; homogeneous, 0), margin (ill-defined, 1; well-defined, 0), cortical integrity (with cortical destruction, 1; without, 0), soft tissue extension (with adjacent tissue involvement, 1; without, 0), and cervical lymph node (with lymphadenopathy, 1;

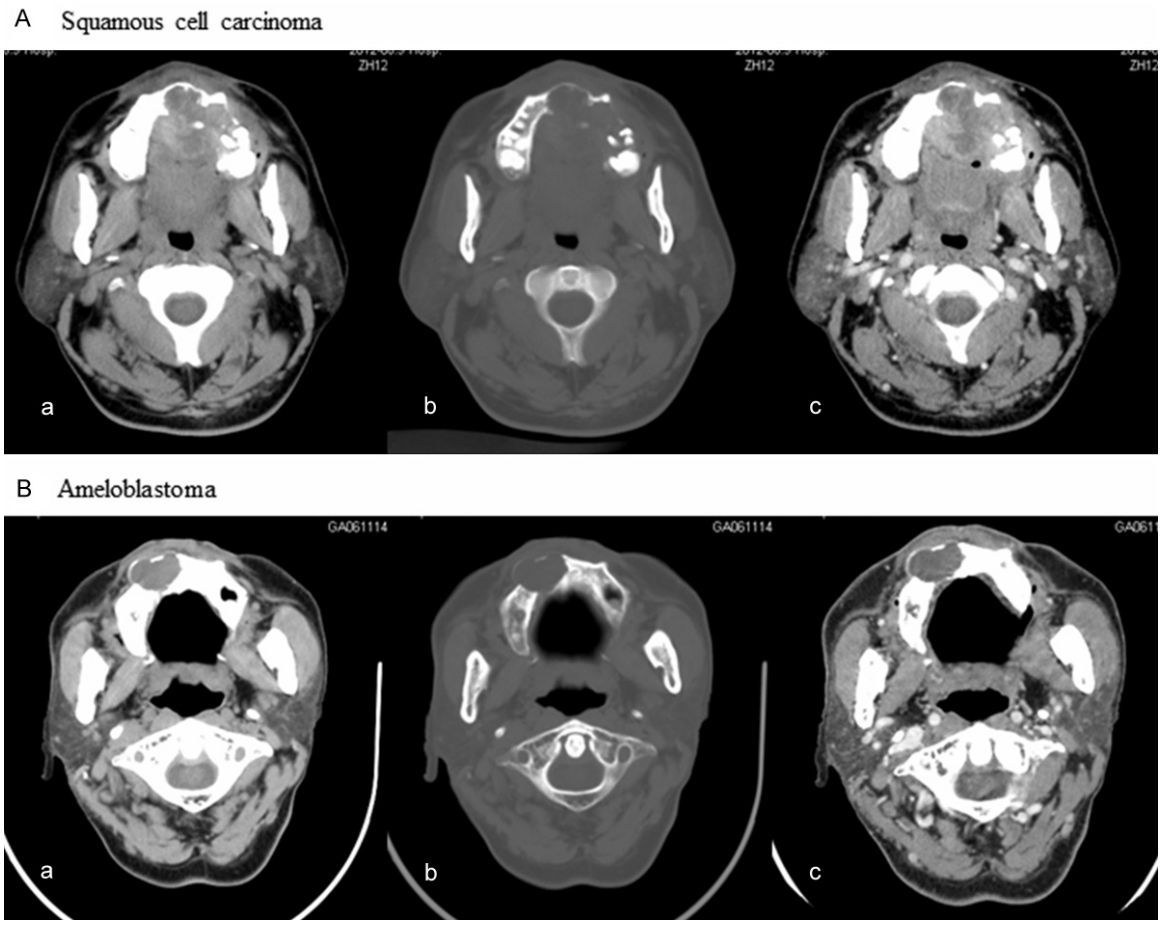

Figure 1. A: Images of squamous cell carcinoma. a: Plain CT (soft tissue window) shows an ill-defined mass in the maxilla with heterogeneous texture and extension into adjacent soft tissue; b: Plain CT (bone window) shows cortical erosion; c: Enhanced CT (soft tissue window) shows heterogeneous enhancement. B: Images of ameloblastomas. a: Plain CT (soft tissue window) shows a well-defined mass with homogeneous texture; b: Plain CT (bone window) shows bone expansion and cortical remodeling; c: Contrast-enhanced CT (soft tissue window) shows no obvious enhancement.

without, 0). The CT characteristic of enhancement was not included in the summed score because some patients underwent plain CT scan only. The scores for the five variates were summed for each lesion. Receiver operating characteristic (ROC) curves were generated to evaluate the diagnostic ability of summed CT score. We plotted the sensitivity versus (1-specificity) for each cut-off value across the range of CT score to generate ROC curve and the areas under the ROC curve (AUC) were assessed. We then triplicatedly classified the patients into three groups and the summed score value on the 33.3% and 66.6% points of score distribution from all lesions were selected as the cut-off values. The ability of the summed scores in differentiating malignant lesions from benign lesions was assessed using logistic regression analysis with adjustment for possible confounding factors.

Results

Patients and clinical characteristics

A total of 322 patients (136 male, 186 female; age: 40.9 ± 20.2 years) with pathologically confirmed maxillary lesions were included. The demographic and clinical characteristics of the patients are summarized in **Table 1**. In 170 of the 322 patients, MMTs were diagnosed, with the most prevalent tumors being osteosarcoma (n = 34), squamous cell carcinoma (n = 31), and adenoid cystic carcinoma (n = 25). In the remaining 152 patients with BMLs, the most prevalent lesions were ameloblastomas (n =

Table 1. Demographic and clinical characteristics of study patients

Characteristics	Malignant maxillary tumor (170) N (%)	Benign maxillary lesion (152) N (%)	*P* value[a]
Mean age ± SD (year)	46.7 ± 18.8	34.6 ± 19.8	< 0.001
Sex			0.652
M	74 (43.5)	62 (40.8)	
F	96 (56.5)	90 (59.2)	
Smoking			0.259
Ever	37 (21.8)	25 (16.4)	
Never	133 (78.2)	126 (83.6)	
Alcohol			0.112
Ever	15 (8.8)	6 (3.9)	
Never	155 (91.2)	145 (96.1)	
Stage			NA
I-II	78 (45.9)	-	
III-IV	92 (54.1)	-	
Treatment			
S	51 (30.0)	148 (97.4)	< 0.001
C	2 (1.2)	-	NA
X	2 (1.2)	-	NA
Other[b]	115 (67.6)	4 (2.6)	

S = surgery; C = chemotherapy; X = radiotherapy; NA = not available. [a]*P* values of χ^2 test (the Fisher exact test was used where appropriate) for categorical variables and unpaired t test for noncategorical data. [b]Combined treatment of surgery and/or chemotherapy and/or radiotherapy.

52), ossifying fibroma (n = 28), and odontoma (n = 15). A significant difference was observed for age ($P < 0.001$) and surgery treatment ($P = 0.049$) between patients with MMT and BML. There was no statistical difference in sex, smoking status, or alcohol use between patients with MMT and BML ($P > 0.05$).

Association between malignancy and CT imaging characteristics

Plain CT images were available for 291 included patients, and 216 of them also had contrast-enhanced CT scans. The patients' CT characteristics are summarized in **Table 2**. The CT characteristics of enhancement, inner texture, margin, cortical integrity, soft tissue extension, and cervical lymphadenopathy were all significantly different between patients with MMTs and BMLs ($P < 0.001$). All MMTs demonstrated enhancement after intravenous injection of contrast agent. After adjusting for age, sex, smoking status, alcohol use, and stage in the logistic regression model, the patients with cortical involvement were approximately 128 times more likely to have MMTs than those without cortical involvement (OR, 128.6, 95% CI, 38.6-428.3). Furthermore, we found that patients with ill-defined margins and soft tissue extension were approximately 60 times more likely to have MMTs than those with well-defined borders and no adjacent structure extension (OR, 58.7, 95% CI, 17.8-193.5 for margin; OR, 62.4, 95% CI, 28.9-134.7 for soft tissue extension). Multivariable analyses further showed that patients with cortical involvement and soft tissue extension were approximately 50 and 18 times more likely to have an MMT than those without cortical destruction or adjacent soft tissue extension (OR, 49.9, 95% CI, 4.4-560.5 for cortical integrity; OR, 17.5, 95% CI, 6.9-44.3 for soft tissue extension), as shown in **Table 3**.

To assess the combined influence of different CT characteristics on the differential diagnosis, multivariate analyses were performed. The AUC of the summed CT scores for differentiating MMTs from BMLs was 0.9341 (**Figure 2**). **Table 4** shows the associations between malignancy and summed CT score. Patients were divided into three groups according to the summed scores of five CT characteristics: (1) score < 2, (2) 2 ≤ score < 4, and (3) score ≥ 4. We found that compared with patients who had a summed CT score of < 2, patients with a score of 2-4 were approximately 20 times more likely to have an MMT (OR, 20.1, 95% CI, 4.3-94.7) and patients with a score ≥ 4 were approximately 430 times more likely to have an MMT (OR, 430.5, 95% CI, 87.6-2015.7).

Discussion

Our current retrospective evaluation of CT results in 291 patients suggests that CT is useful in discriminating malignant maxillary lesions from benign ones. Belkin et al. [9] compared MRI and CT images of benign and malignant lesions of the maxilla and mandible in a group

Table 2. Univariate analysis of associations between CT characteristics and malignancy

Characteristics	Malignant maxillary tumor (159) N (%)	Benign maxillary lesion (132) N (%)	*P* value[a]	β value	OR (95% CI)
Enhancement[b]			< 0.001		
No	0	24 (35.8)			
Yes	149 (100.0)	43 (64.2)			NA
Inner texture			< 0.001		
Homogeneous	5 (3.1)	29 (22.0)			1.0
Heterogeneous	154 (96.9)	103 (78.0)		2.2	8.7 (3.3-23.1)
Margin			< 0.001		
Well-defined	3 (1.9)	70 (53.0)			1.0
Ill-defined	156 (98.1)	62 (47.0)		4.1	58.7 (17.8-193.5)
Cortical Integrity			< 0.001		
No	3 (1.9)	94 (71.2)			1.0
Yes	156 (98.1)	38 (28.8)		4.9	128.6 (38.6-428.3)
Soft tissue extension			< 0.001		
No	26 (16.4)	122 (92.4)			1.0
Yes	133 (83.6)	10 (7.6)		4.1	62.4 (28.9-134.7)
Lymphadenopathy			< 0.001		
No	128 (80.5)	128 (97.0)			1.0
Yes	31 (19.5)	4 (3.0)		2.0	7.7 (2.6-22.4)

CI = confidence interval; OR = odds ratio; NA = not available. [a]*P* values of χ^2 test (the Fisher exact test was used where appropriate) for categorical variables and unpaired *t* test for noncategorical data. [b]Enhancement was not available in 10 malignant and 65 benign cases, which underwent plain CT only.

Table 3. Multivariable analysis of associations between CT characteristics and malignancy

Characteristics	Malignant maxillary tumor (159) N (%)	Benign maxillary lesion (132) N (%)	β value	Adjusted OR[a] (95% CI)
Inner texture				
Homogeneous	5 (3.1)	29 (22.0)		1.0
Heterogeneous	154 (96.9)	103 (78.0)	1.2	3.4 (0.8-15.3)
Margin				
Well-defined	3 (1.9)	70 (53.0)		1.0
Ill-defined	156 (98.1)	62 (47.0)	1.1	0.3 (0.02-4.4)
Cortical integrity				
No	3 (1.9)	94 (71.2)		1.0
Yes	156 (98.1)	38 (28.8)	3.9	49.9 (4.4-560.5)
Soft tissue extension				
No	26 (16.4)	122 (92.4)		1.0
Yes	133 (83.6)	10 (7.6)	2.9	17.5 (6.9-44.3)
Lymphadenopathy				
No	128 (80.5)	128 (97.0)		1.0
Yes	31 (19.5)	4 (3.0)	1.5	4.4 (0.8-24.5)

CI = confidence interval; OR = odds ratio. [a]Adjusted for age, sex, smoking status, alcohol use, and stage in a logistic regression model.

of 16 patients. They reported that CT was equal or superior to MRI in lesion detection and in the evaluation of cortical involvement, while MRI was superior in the evaluation of lesion margins and soft tissue extension of diseases. In the current study, we chose to focus on CT imaging

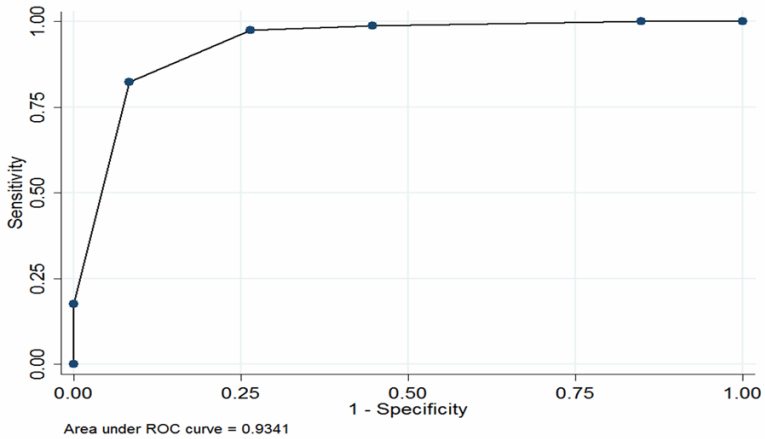

Figure 2. The plot of a receiver-operating characteristic (ROC) curve. The average area under the curve (AUC) of 0.934 denotes the accuracy of the signature of CT characteristics in the test dataset. The ROC curve depicts a true positive rate (sensitivity) versus a false positive rate (one minus specificity).

Table 4. Combined effects of CT characteristics on malignancy

Summed CT score	Malignant maxillary tumor (159) N (%)	Benign maxillary lesion (132) N (%)	β value	Adjusted OR[a] (95% CI)
< 2[b]	2 (1.3)	73 (55.3)		1.0
2-4	26 (16.2)	48 (36.4)	3.0	20.1 (4.3-94.7)
≥ 4	131 (82.4)	11 (8.3)	6.1	430.5 (87.6-2015.7)
Trend				< 0.001

CI = confidence interval; OR = odds ratio. [a]Adjusted for age, sex, smoking status, alcohol use, and stage in a logistic regression model. [b]Reference group.

because it has better clinical applicability and cost-effectiveness than MRI. Other disadvantages of MRI include patient intolerance secondary to claustrophobia and the inability to image patients who have pacemakers or ferromagnetic surgical clips. In addition, lack of signal from cortical bone on MRI may result in a loss of information regarding extent of disease. MRI is also less sensitive in the detection of small areas of calcification, ossification, and air because its spatial resolution is slightly less than that of CT. Although the superior soft tissue contrast of MRI could make it a useful modality for analyzing the internal structures of a lesion and the soft tissue extension, in the current study, we found that the CT manifestations of ill-defined margin, cortical involvement, and adjacent soft tissue invasion were significantly associated with malignancy, which confirms the ability of CT to evaluate these lesions and the invasion of adjacent soft tissue. However, further studies in large cohorts of patients are still needed to evaluate and compare the ability of different imaging modalities to discriminate malignant lesions of the maxilla.

In our study, we examined whether CT characteristics such as the inner texture of the lesion, delineation of the margin, cortical integrity of the maxilla, and extension into adjacent soft tissue could be used to determine whether a lesion was benign or malignant. In general, lesions with well-defined borders are usually benign, whereas lesions with ill-defined borders invariably represent aggressive, inflammatory, or neoplastic processes. Slow-growing lesions often cause expansion with cortical bowing, while cortical destruction denotes aggressive inflammatory or neoplastic lesions [12]. Belkin et al. [9] reported that CT imaging reliably demonstrated sharp, well-demarcated margins in benign lesions and irregular and indistinct margins in malignancy. In the current study, the CT findings for enhancement, inner lesion texture, margin, cortical involvement, soft tissue extension, and lymphadenopathy were all significantly different between the malignant and benign maxillary lesions. We found that the most useful CT features in the differentiation of malignant and benign lesions are the presence of cortical destruction and adjacent soft tissue invasion; both are effects of a lesion on the surrounding structure, which helps in inferring the behavior of the lesion. In our scoring system, a lesion with four or five positive CT findings would be 430 times more likely to be malignant than one with 1 or 0 positive CT findings. The area under the curve of combined CT scores for differentiating malignant maxillary tumors was 0.9341. These results are promising and further confirm the value of CT for the differential diagnosis of malignant lesions in the maxilla.

Although the current study reveals significant associations between CT characteristics and

maxillary malignancy, it has some limitations. First, details on lesion location and size are lacking because many of the lesions were scattered or diffuse with no clear border. Second, the disease distribution in our study may not reflect that in the general population because we only included patients with histopathologically confirmed, previously untreated maxillary lesions. Patients who receive a definitive diagnosis after clinical and X-ray examination or without planning for surgical treatment might not undergo CT and biopsy for a histopathological diagnosis. Third, we did not include all the manifestations on CT images that might be suggestive of the nature of the lesion. For example, some types of periosteal reactions are quite specific, like the sunburst type in osteosarcoma; and widening of the inferior alveolar canal with maintenance of a cortical boundary may indicate the presence of a benign lesion of vascular or neural origin. We chose to evaluate the CT characteristics that are relatively easy to assess, more universally applicable, and not specific to a particular disease. Finally, the demographic, clinical and radiological data for the cohort were collected retrospectively from one institution. Thus, future prospective and multi-center studies with larger sample sizes are needed to validate our findings.

In conclusion, the morphologic characteristics on CT images provide valuable clues for discriminating malignant lesions of the maxilla from benign ones and the most useful features of malignancy in the differential diagnosis are the presence of cortical involvement and soft tissue extension. Moreover, the value of multiparametric CT may highly increase such a differential diagnosis. However, larger studies are needed to validate our findings.

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Disclosure of conflict of interest

None.

Abbreviations

AUC, areas under the ROC curve; BML, benign maxillary lesions; CI, confidence interval; CT, computed tomography; FOV, field of view; MMT, malignant maxillary tumors; MRI, magnetic resonance imaging; OR, odds ratio; ROC, receiver operating characteristic.

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