

Middle turbinate edema as a diagnostic marker of inhalant allergy

Aneeza W. Hamizan, MD^{1,2}, Jenna M. Christensen, PhD¹, Jareen Ebenzer, MD¹, Gretchen Oakley, MD¹, Jessica Tattersall, MBBS (Hons)¹, Raymond Sacks, MD^{3,4} and Richard J. Harvey, MD, PhD^{1,3}

Background: Middle turbinate edema could be a characteristic feature of aeroallergen sensitization. In this study we sought to determine the diagnostic characteristics of middle turbinate edema as a marker of inhalant allergy.

Methods: A cross-sectional diagnostic study was performed on patients who had undergone nasal endoscopy and allergy testing. Allergy status was determined by positive serology or epicutaneous testing. Endoscopy was reviewed by blinded assessors for middle turbinate head edema. Appearance was graded as either normal, focal, multifocal, diffuse, or polypoid edema. Receiver-operator (ROC) analysis, likelihood ratio (LR), sensitivity, specificity, and positive predictive value (PPV) were determined.

Results: One hundred eighty-seven patients representing 304 nasal cavities were assessed (42% female, age 39.74 ± 14.7 years, 57% allergic). Diffuse edema (PPV 91.7%/LR = 8) and polypoid edema (PPV 88.9%/LR = 6.2) demonstrated

the strongest association with inhalant allergy. Multifocal edema was used as a cut-off to represent inhalant allergy from ROC analysis, which demonstrated 94.7% specificity and 23.4% sensitivity. The PPV for multifocal was 85.1% and LR = 4.4.

Conclusion: Middle turbinate edema is a useful nasal endoscopic feature to predict presence of inhalant allergy and, although not sensitive, has excellent PPV. © 2016 ARS-AAOA, LLC.

Key Words:

allergic; atopy; endoscopy; middle turbinate; nasal polyp; rhinitis; turbinates

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Allergic and nonallergic rhinitis are differentiated by systemic evaluation using either a skin prick test or serologic test for specific immunoglobulin E (IgE). It remains unclear whether these atopic markers are responsible for the symptoms of rhinitis. These systemic tests for atopy,

although sensitive, do not detect local allergic inflammation in the nose. This localized form of allergic rhinitis is termed *entopy* or *local allergic rhinitis*. A simple and specific test is needed for rhinitis.

Nasal endoscopy is a simple procedure that allows easy visualization of the nasal cavity. The presence of a pale, hypertrophied inferior turbinate head, cobblestoning of mucosa, and congestion are hallmark endoscopic features of allergic rhinitis. However, their diagnostic characteristics are not well described. Recently, edema on the leading edge of the middle turbinate head was found to be a promising endoscopic feature of allergic rhinitis.¹ The head of the middle turbinate or the most anterior portion of the middle turbinate is a likely site for allergen deposition. In allergic patients, inhaled aeroallergens are deposited onto the head of the middle turbinate, which triggers local allergic inflammation and leads to mucosal edema. White et al.¹ found middle turbinate polypoid edema to be completely associated with inhalant allergy. Among 16 patients with middle turbinate polypoid edema not involving the ethmoid, all had a positive allergy test to aeroallergen. Therefore, middle turbinate head edema could be a specific diagnostic feature that differentiates between allergic and nonallergic

¹Rhinology and Skull Base Research Group, St. Vincent's Centre for Applied Medical Research, University of New South Wales, Sydney, NSW, Australia; ²Department of Otolaryngology-Head and Neck Surgery, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia; ³Australian School of Advanced Medicine, Macquarie University, Sydney, Australia; ⁴Department of Otolaryngology, Head and Neck Surgery, Concord General Hospital, University of Sydney, Sydney, NSW, Australia

Correspondence to: Aneeza W. Hamizan, MD, 67 Burton Street, Darlinghurst, NSW 2010, Australia; e-mail: draneeza@gmail.com

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rhinitis. In this study we sought to determine the diagnostic characteristics of middle turbinate edema as a marker of inhalant allergy among patients with rhinitis. The tail or posterior end inferior turbinate (mulberry hypertrophy) is also investigated.

Patients and methods

A cross-sectional diagnostic study was performed on patients diagnosed with rhinitis and a negative computed tomography scan, which excluded sinus involvement. All patients had both endoscopy and allergy assessment. The study was approved by the local human research ethics committee (HREC-SVH09/083). Informed consent was obtained from all participants.

Study population

Patients who had undergone nasal endoscopy and allergy testing at a tertiary referral clinic were assessed. Consecutive patients were included if they had both endoscopy images and documentation of allergy status. All included patients had rhinitis symptoms of at least nasal obstruction and were to undergo turbinate (with or without septal) surgery. Allergy assessment was performed by epicutaneous challenge or serology immunocap analysis. Those with both symptoms and a positive allergy assessment were considered the “allergic” group.² Allergy assessments, either from a skin prick test or serology and endoscopy, were performed within 6 months of each other. Patients were excluded if there was evidence of prior middle turbinate surgery (scarred or cut middle turbinate) on endoscopy. Patients were excluded if they had systemic conditions believed to affect mucosa, namely immunodeficiency, vasculitis, cystic fibrosis, or granulomatous disease.

Asthma status was determined by either positive spirometry result on challenge testing or β -agonist use, or if currently using regular inhaled bronchodilator or corticosteroid therapy. Smokers were defined those currently smoking or having ceased within the last 12 months.

The use of any drugs that may influence turbinate edema was documented. These included oral or intranasal steroids, antireflux medications, and other immunosuppressants.

Allergy status

Allergy status, or aeroallergen sensitization, was defined by either serologic assessment or epicutaneous challenge. For serologic assessment, serum specific immunoglobulin E (IgE) to 4 allergen mixes was evaluated (dust mite, mold, animal, and grass). The house dust allergen mix tested for *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, and *Blattella germanica*; the mold mix for *Penicillium chrysogenum*, *Cladosporium herbarum*, *Aspergillus fumigatus*, and *Alternaria alternata*; the epithelial mix for cat, horse, cow, and dog dander; and the grass mix for *Cynodon dactylon*, *Lolium perenne*, *Phleum pratense*, *Poa pratensis*,

Sorghum halepense, and *Paspalum notatum*. Serum specific IgE (>0.35 KU/L) for any 4 of the mixed airborne antigens was considered positive.

Epicutaneous allergy assessment was performed by a skin prick test. Allergens in a 50% glycerin solution were applied to the volar forearm with a Multi-Test II device (Lincoln Diagnostics, Decatur, IL). Evaluation was done on a panel of 16 allergens that corresponded to the 4 allergen mixes (dust mite, mold, animal, and grass). A negative glycerin control and positive histamine control were used. The wheal size was measured 15 minutes after application. A positive skin test result was defined as a wheal of >3 mm to any 1 of the allergens with a nonreactive negative control. Patients refrained from antihistamines for at least 72 hours prior to testing. Patients were grouped as allergic or nonallergic if either serology or skin prick test was positive.

Endoscopic assessment

Images assessed were taken from digital archives from the patient clinic assessments. All patients assessed at our clinic have archived endoscopic assessments. Patients' noses were decongested for the nasal endoscopic assessment with 0.5% phenylephrine/5% lignocaine as a 0.3-mL dose and for at least 5 minutes. The images were assessed for middle turbinate head edema and inferior turbinate tail hypertrophy. Two trained otolaryngologists reviewed the images and graded accordingly guided by the reference images (Figure 1). The assessors were blinded to the allergy status of the patient and their presenting symptoms. For interobserver variability, an independent assessor reviewed a group of patients for interobserver correlations. For intraobserver variability, the original assessor also rescored the same group 8 weeks later.

Middle turbinate edema grading

The appearance of middle turbinate head was graded using a 5-category scale with increasing severity of edema (Figure 1). Categories included normal, focal, multifocal, diffuse, or polypoid edema. Appearance of edema of the middle turbinate was defined as a smooth, semiluent, jellylike protrusion from the mucosa. Normal was defined as solid pink-to-red mucosa without any clearness, translucency, or nodularity of the surface. Focal edema was defined as the presence of any translucent nodularity on the leading edge of middle turbinate fully surrounded by normal mucosa. Multifocal edema was defined as the presence of >1 translucent nodule, fully surrounded by normal mucosa. Diffuse edema was defined as a translucent, jellylike mucosal surface occupying the entire leading edge of the middle turbinate mucosa without any intervening normal mucosa. Polypoid edema was defined as a grapelike, translucent protrusion hanging beyond the leading edge of the middle turbinate mucosa.

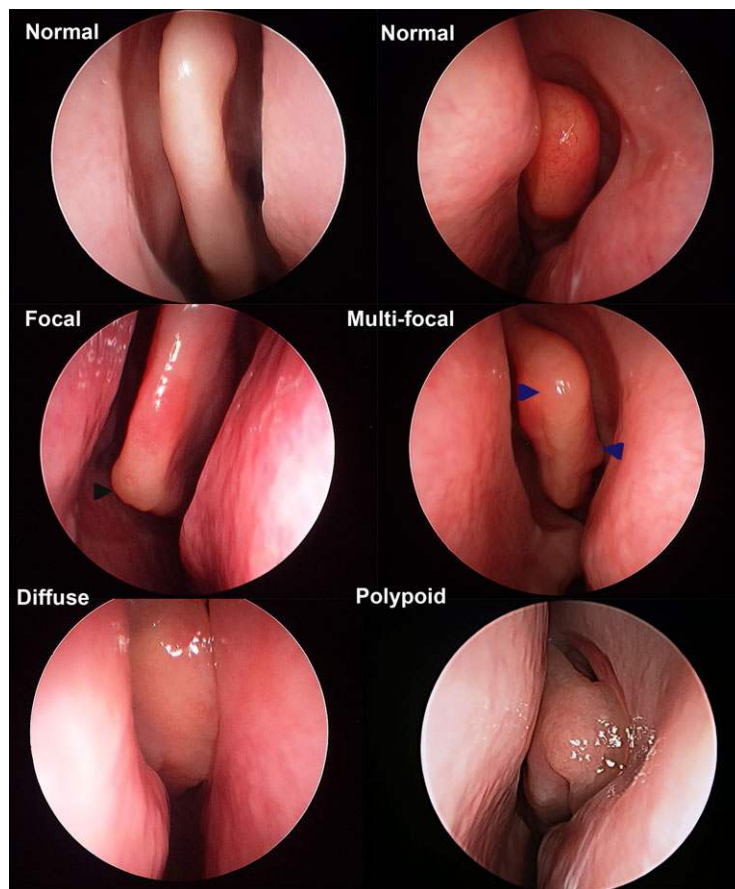


FIGURE 1. The reference image used by study-blind assessors for grading of middle turbinate head edema. Normal: normal mucosa with a smooth pink surface, without jellylike nodularity. Focal edema: translucent nodularity completely surrounded by normal mucosa (blue arrowheads). Multifocal edema: edema (black arrowheads) with more than 1 nodularity, each surrounded by normal mucosa. Diffuse edema: entire leading edge of middle turbinate covered in jellylike translucency. Polypoid edema: teardrop projection of mucosa beyond the leading edge of the middle turbinate.

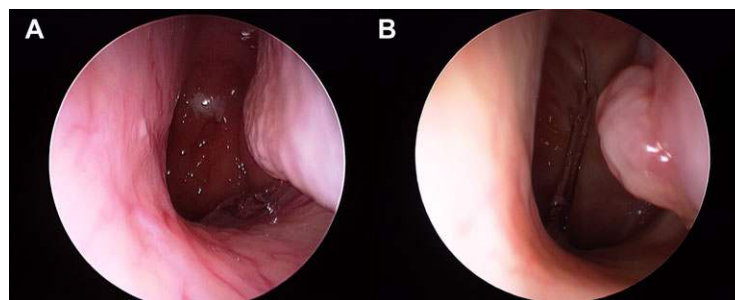


FIGURE 2. The reference images used by blinded assessors to grade the posterior end of the inferior turbinate. Normal inferior turbinate tail (A) and inferior turbinate tail hypertrophy (B) where the bulky soft tissue begins at the waist and expands posteriorly.

Inferior turbinate hypertrophy

The inferior turbinate tail was graded as either normal or mulberry. A *mulberry tail* was defined as a bulky posterior soft-tissue component of the inferior turbinate. This bulky tail needed to have waist where the diameter expanded posteriorly beyond the anterior body (Figure 2).

Statistical analysis

Statistical analyses were performed using SPSS version 20.0 (SPSS, Inc., Chicago, IL). In comparing baseline values

between allergic and nonallergic groups, continuous data were assessed parametrically and compared using Student's *t* test. Comparisons of proportions were performed using chi-square analysis. Fisher's exact test was used for drug intake of oral steroids and immunosuppressants, as there were <5 patients in 2 or more of the categories. When assessing middle turbinate grades, Kendall's tau-b was used to test for an association between middle turbinate edema and allergy status. The analysis was done for each nasal cavity assessed on endoscopy. In assessing the association

TABLE 1. Comparison of baseline characteristics between allergic and nonallergic groups

	Nonallergic	Allergic	<i>p</i> value
Patients (n)	81	106	—
Age (mean ± SD)	44.31 ± 14.94	36.25 ± 13.64	<0.01
Gender (% female)	20.3	21.9	0.26
Smokers (%)	1.6	5.3	0.16
Asthma (%)	5.9	21.9	<0.01
Medication use			
Intranasal corticosteroids	4.3	9.7	0.22
Oral corticosteroids	2 (1.1)	1 (0.5)	0.57
Immunosuppressants	1 (0.5)	0 (0.0)	0.41
Reflux medications	4 (2.1)	6 (3.2)	1.00

SD = standard deviation.

between inferior turbinate tail grade and allergy status, the chi-square test was used. Likelihood ratios (LRs), sensitivity, specificity, and positive predictive value (PPV) were determined for middle turbinate head grades and inferior turbinate hypertrophy. When calculating these values, the patients were defined as a threshold at each grade. Receiver-operating characteristic (ROC) curves were used to define an optimal middle turbinate head edema grade. Inter- and intraobserver reliability was assessed using the intraclass correlation coefficient (ICC). $p < 0.05$ was considered significant.

Results

One hundred eighty-seven patients representing 304 nasal airways (age [mean ± SD] 39.74 ± 14.7 years, 42% female) were included for assessment. Of these, 56.7% were defined as allergic. Among the allergic patients, 59.4% were sensitized to more than 1 allergen group. In those sensitized, the most prevalent aeroallergen was dust mix (82.1%), followed by grass mix (57.5%), animal epithelium mix (30.1%), and then mold (16.9%).

Among the patient population, 6.9% smoked and 27.8% were known to have asthma. Only a small number of patients were taking antireflux medications (5.3%), intranasal corticosteroids (13.9%), oral steroids (1.6%), or other immunosuppressant (0.5%). Allergic patients were more likely to be younger (36.25 ± 13.64 years vs 44.31 ± 14.94 years, $p < 0.01$), and the prevalence of asthma was higher (21.9% vs 5.9%, $p < 0.01$). There were no significant differences in baseline characteristics and drug use between patients with and without allergy, except for asthma status and age (Table 1).

Middle turbinate head edema

The overall incidence of any middle turbinate edema was 28.6%. The rate of middle turbinate edema was 32.9%

TABLE 2. Comparison of middle turbinate head edema grades between allergic and nonallergic groups

	Nonallergic	Allergic
Nasal cavities (n)	133	171
Normal (%)	33.9	37.5
Focal edema (%)	7.6	5.6
Multifocal edema (%)	1.6	5.9
Diffuse edema (%)	0.01	4.6
Polypoid edema (%)	0.03	2.6

Kendall's tau-b: $p < 0.01$.

among the allergic rhinitis patients, which included focal edema (46%), multifocal (27%), diffuse edema (17%), and polypoid edema (10%). Middle turbinate head grades were associated with allergy status (Kendall tau-b, $p < 0.01$) (Table 2).

The sensitivity of each grade of middle turbinate edema was poor: focal edema, 27%; multifocal edema, 23.4%; diffuse edema, 10.4%; and polypoid edema, 3.7%. However, specificity was high: focal edema, 81.3%; multifocal edema, 94.7%; diffuse edema, 98.7%; and polypoid edema, 99.4%. This resulted in excellent PPVs for all grades, except for focal edema (focal edema PPV = 65.5%, multifocal edema PPV = 85.1%, diffuse edema PPV = 91.7%, and polypoid edema PPV = 88.9%). The LR for the diagnosis of positive allergy status was multifocal edema (LR = 4.4), diffuse edema (LR = 8.0), and polypoid edema (LR = 6.2).

ROC curve analysis (Figure 3) defined multifocal edema as a cut-off to predict allergic status, with area under curve (AUC) 0.57 (95% confidence interval [CI], 0.509 to 0.637; $p = 0.03$). Multifocal edema demonstrated 94.7% specificity, 23.4% sensitivity, 85.1% PPV, and LR = 4.4. Diffuse edema showed 98.7% specificity, 10.4% sensitivity, 91.7% PPV, and LR = 8.0, which defined the allergy status well, but lacked sensitivity.

Inferior turbinate tail hypertrophy

Of the inferior turbinate tails assessed, 15.9% had a mulberry or hypertrophic appearance. There was no significant association of inferior turbinate tail hypertrophy with allergic status in our study population (6.8% vs 9.1%, $p = 0.49$). The sensitivity for mulberry hypertrophy to predict allergy status was 13.3%, with specificity 81.4%, 42.9% PPV, and LR = 0.72.

Inter- and intraobserver reliability

Two independent observers graded middle turbinate head edema in 53 patients. The interobserver ICC (95% CI) for middle turbinate head edema grade was 0.92 (95% CI, 0.88 to 0.93). The ICC for intraobserver reliability was 0.99 (95% CI, 0.98 to 0.99).

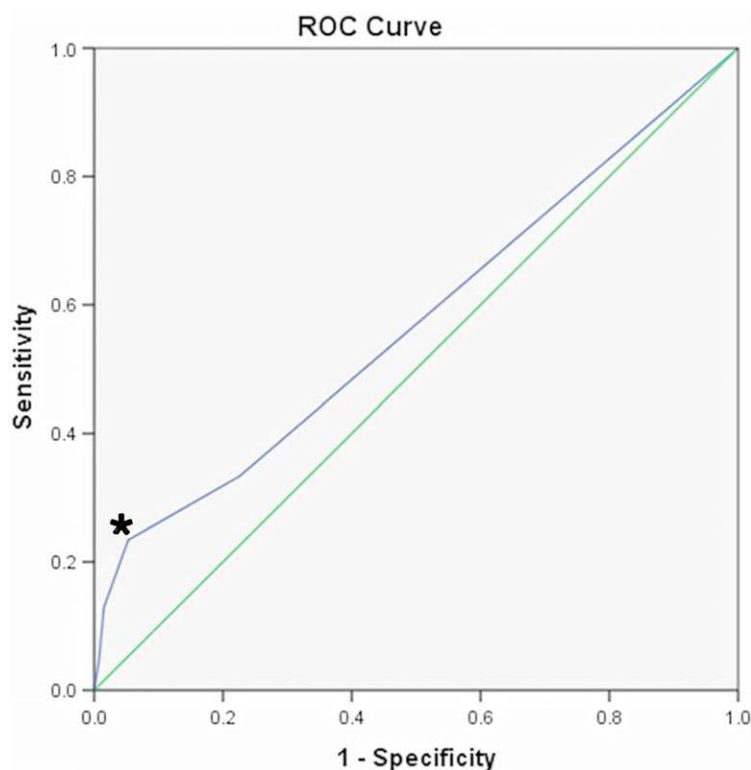


FIGURE 3. Receiver-operating characteristic analysis for middle turbinate edema and event of allergy (area under curve, 0.57; 95% confidence interval, 0.509 to 0.637; $p = 0.03$). Multifocal edema grade (*) has 94.7% specificity, 23.4% sensitivity, 85.1% PPV, and LR = 4.4.

Discussion

Although the overall incidence of middle turbinate head edema was demonstrable in only 28.6% of nasal cavities, this included patients with nonallergic rhinitis in whom edema would not necessarily be expected. In patients with allergy, the frequency of middle turbinate edema was slightly higher (32.9%), similar to that in allergic patients not using intranasal corticosteroids (32.7%). The middle turbinate edema test is specific with good PPV, but it not a sensitive test for allergic rhinitis.

Frank polypoid degeneration of the middle turbinate independent of any sinus disease was present in 3% of the nasal cavity as demonstrated by a patient (Figure 4). White et al.¹ described a complete association between isolated polypoid middle turbinate without any ethmoid involvement to inhalant allergy. It is not known why the middle turbinate mucosa develops polyps as compared with the hypertrophied inferior turbinate. An embryologic difference has been postulated as a reason why inferior turbinate is a bone of its own whereas the middle turbinate is part of the ethmoid bone.¹ This could account for the differing responses to inflammation.

In this study, instances of edema of the middle turbinate head from the focal edematous area to frank polyps were evaluated to determine whether a relationship with inhalant allergy sensitization could be determined. All grades were found to be highly specific for allergy and improved with increased edema grade. Ameli et al.³ found a significant

association between middle turbinate head contact point and allergy among children with rhinitis. They also found that children with a middle turbinate contact point with adjacent structures had an increased risk of allergy (odds ratio, 3.32; 95% CI, 1.51 to 7.27) and a PPV of 86.2%. This finding is similar to our study, where multifocal edema as a threshold had a PPV of 85.1%. Therefore, multifocal edema (or diffuse edema) could be a useful marker for inhalant allergy among rhinitis patients.

Among the 14.7% of patients who were above the threshold of multifocal edema, 14.9% were classified as nonallergics, based on epicutaneous or serologic assessment. It is possible that these patients may have had local allergic rhinitis or alternate inflammatory rhinitis. The high specificity of middle turbinate edema, especially diffuse and polypoid edema, makes it a potentially useful diagnostic tool for local allergic rhinitis and an area for further research.

Overall, there was poor sensitivity for middle turbinate head edema. Edema in the nasal cavity is easily influenced by anti-inflammatory drugs or anatomic variation, which can reduce its appearance. Mucosal edema may also be caused by other nonspecific stimuli, such as trauma from previous instrumentation, infection, or environmental or chemical irritation. This applies mostly to focal edema, which was the least specific. Middle turbinate head edema is a very specific finding for allergy and is not a sensitive tool. Although concomitant use of intranasal corticosteroid



FIGURE 4. Nasal endoscopy image of a patient with extensive polypoid edema isolated to middle turbinate extending almost to the left nasal vestibule (A). Coronal computed tomography scan shows polypoid edema at the same location (B), but the corresponding ipsilateral ethmoid and sinus cavity is unaffected by disease (C).


(INCS) spray might have reduced the prevalence of edema on endoscopy, the use of INCS between groups was similar (allergic rhinitis 9.7% vs nonallergic rhinitis 4.3%, $p = 0.22$). Even if INCS use was significantly higher in the allergic group, this would have only have reduced middle turbinate edema test characteristics. It may be possible that the presence of middle turbinate edema has a higher sensitivity than what has been reported.

The middle turbinate head grading system that was assessed appeared to have good test characteristics. Both inter- and intraobserver ICCs were good and it is likely that the use of reference images and predefining the appearance of edema contributed to this finding. Middle turbinate edema may be difficult to assess and may be confused with a pale-looking turbinate. McCoul et al.⁴ graded middle turbinate mucosa edema as either normal, edema, or polypoid among post-sinus surgery patients and found poor interrater agreement. Prior surgery around the middle turbinate may make it difficult to determine allergic changes.

Mulberry hypertrophy of inferior turbinate has long been associated with allergy. It has been described in textbooks

since the 1700s, but it was Wallner et al.⁵ who first studied its association with allergy in 1949. Using mirror posterior rhinoscopy to detect mulberry hypertrophy, he found it to be associated with allergic rhinitis. Eren et al.⁶ found polypoid degeneration of the inferior turbinate tail to be 100% specific, but only 1.5% sensitive. In our study, there was no association between mulberry hypertrophy and allergy, which also had poor PPV and positive LR. It is possible that only well-developed, late hypertrophic changes of the allergic turbinate are associated with allergy. Brook et al.⁷ compared the appearance of the posterior end of the inferior turbinate between atopic and nonatopic patients with rhinitis symptoms and did not find any significant difference.

Conclusion

Middle turbinate edema, although not a sensitive marker, is highly specific for the presence of inhalant allergy, with excellent PPV and LR for making the diagnosis of allergy sensitization. It has potential for use as a marker for local inhalant allergy as it is both simple and reliable. 

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