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Use of FENO in etiological diagnosis of small airway diseases

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ABSTRACT

Although major progress has been achieved in the recognition of small airways (SMA) disease, diagnosis still remains difficult. The analysis of FeNO has recently become of great interest in the diagnosis and monitoring of many respiratory diseases. This study focused on value of FeNO in etiological diagnosis of SMA diseases and correlation of FeNO values with spirometry variables.

SUMMERY. FeNO is an important biomarker in assessing of the etiology of respiratory symptoms. The difference between values of FeNO in asthma and other diseases with SMA obstruction is significant.

KEYWORDS : FeNO, small airways, asthma.

INTRODUCTION

There is an increased interest in SMA disease, and some new insights have been gained about the contribution of these SMA to the clinical expression of respiratory diseases *(Van den Berge et al.2011)*.Fig1

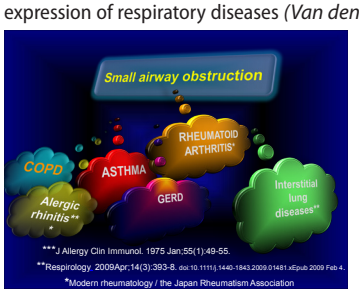

Figure 1. Diseases with SMA obstruction

In the 1960s Weibel proposed a structural model of the airways *(Weibel, 1979)*. The SMA zone (airways < 2 mm inner diameter in adults), also referred to as the peripheral airways, starts around the eighth generation. The obstruction of SMA can occur through a number of mechanisms, including luminal occlusion by mucus, reduction in luminal diameter from inflammatory infiltrates, smooth muscle hypertrophy, or airway wall thickening**.** *(* McNulty* & Usmani, 2014*)*.Fig 2

Unfortunately, no test is yet available that has all the requested features to diagnose, weigh, and monitor SMA diseases in clinical practice. *(Van den Berge et al.2011)***.** Flow measures commonly used in small airway studies are forced expiratory flow rates at 50% (FEF 50%) and at 25% to 75% of vital capacity (FEF 25%-75%). *(Bar-Yishay et al.2003)* The diseases that affect the SMA are difficult to detect by traditional diagnostic tests *(Hansell, 2001)***.**

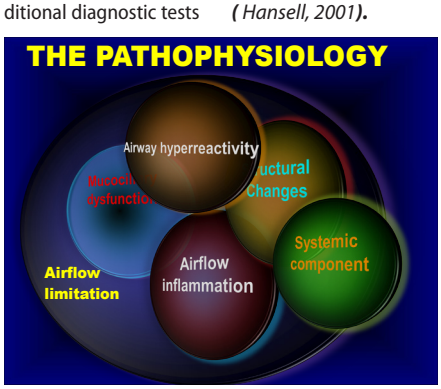

Figure 2. The Pathophysiology of SMA diseases

Peripheral airway inflammation can be examined by measuring nitric oxide concentrations in single breath exhaled air during different fl ow rates. *(Tsoukias &, George, 1998)* There are a few studies in adults assessing the association between SMA function and FeNO in asthma. Exhaled nitric oxide (FeNO) exhibits flow rate dependency, with an inverse correlation between flow rate and FENO *(*Silkoff et al. 1997*)***.*** Patients with chronic cough that is not attributable to asthma have lower NO values than patients with asthma *(Chatkin et al.1999, Dupont et al. 1998)***,** including those with cough caused by gastroesophageal reflux (GERD) *(Parameswaran et al.1998)*. Measurement of FeNO may therefore be a useful screening procedure for patients with chronic cough and would readily identify those patients with cough caused by asthma (*Chatkin et al.1999* ***)***.

FeNO was the first useful non-invasive marker of airway inflammation in asthma and still is the most widely used.

PURPOSE OF THE STUDY

- To study the practical utility of FENO values in the diagnosis and management of diseases with obstruction of the SMA
- To study the correlation of FeNO values with the degree of obstruction in Asthma and COPD.
- To use FeNO to assess the contribution of SMA inflammation and dysfunction in asthma .
- To study the correlation of FeNO values with spirometry variables.

MATERIALS AND METHOD

This prospective diagnostic study was performed between June 2012 and August 2013 in University Hospital "Shefqet Ndroqi", TIRANA, Albania

In total, 252 subjects participated in the studies : 89 with Asthma, 70 with COPD, 34 with Bronchectazi, 33 with GERD, 26 with Sarcoidosis. 71 subjects were with obstruction of SMA.

FENO was measured by an electrochemical nitric oxide analyzer (NIOX MINO; Aerocrine AB, Solna, Sweden). FENO50 was measured according to the ATS/ERS recommendations. *(*ATS/ERS,2005*)***.**

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS16. Comparisons of mean FENO values between the groups were performed by ANOVA and unpaired t tests.Paired samples t-test. Pearson's correlation coefficients were calculated to determine the correlation between the FENO values and continuous data.

RESULTS Among the 71 subjects with obstruction of SMA: 31 with Asthma, 14 with GERD, 11 with COPD, 9 with Bronchiectasis and 6 with Sarcoidosis. Fig 3.

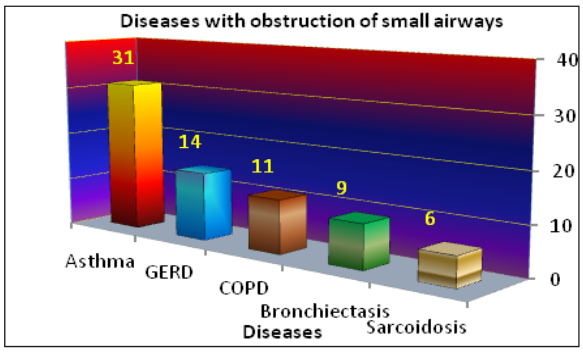

Figure 3. Diseases with obstruction of SMA

- The mean of FeNO in Asthma 37.8 ± 35.8 SD Fig 4
- The mean of FeNO in bronchiectasis 11.2 ± 4.73 SD
- The mean of FeNO in COPD 11.3 ± 8.7 SD
- The mean of FeNO in GERD 12 ± 5.5 SD
- The mean of FeNO in Sarcoidosis 8 ± 3.5 SD

The difference between values of FeNO is significant. ANOVA F -ratio= 5.2 p<0.001

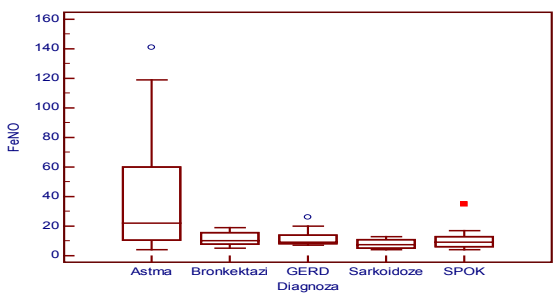

Figure 4. The mean of FeNO value in patients with SMA obstruction

For patients with Asthma

Level	N	Mean	StDev
Normal	11	43.09	± 21.84 SD
Small airways	31	37.84	± 35.81 SD
Mild	13	88.15	± 80.79 SD
Moderate	16	45.44	± 38.78 SD
Severe	14	51.50	±36.53 SD
Very severe	4	21.75	± 9.32 SD

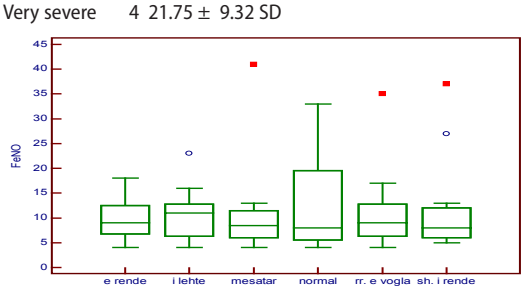

Figure 5.The mean of FeNO value in patients with asthma.

Significant change of the mean of FeNO in asthma with SMA M=37.84 (±35.81) only with FeNO in asthma with mild obstruction F=2.81 p=0.02. Fig 5

For patients with COPD

Level	N	Mean
Normal	5	13.2
Small airways	11	11.3
Mild	11	10.9
Moderate	16	10.4
Severe	13	9.5
Very severe	14	11.5

No significant difference ANOVA F-ratio =0.2 p=0.9 Fig. 6

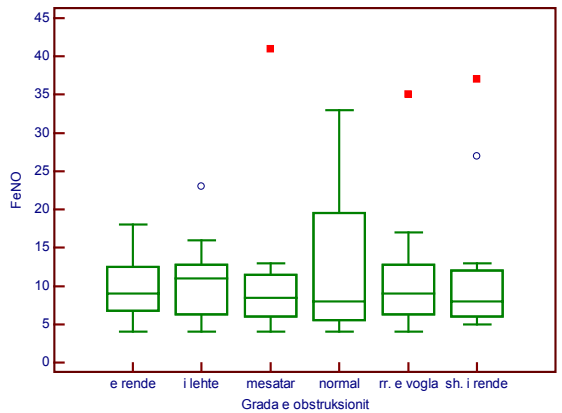

Figure 6. The mean of FeNO value in patients with COPD

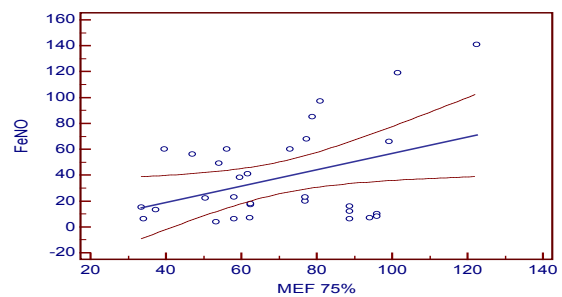

Figure 7. Correlation between of FeNO values and MEF 75 in Asthma with SMA obstruction.

y = -6.2530 + 0.6300 x (r= -0.40 p=0.2) Significant positive correlation Fig 7.

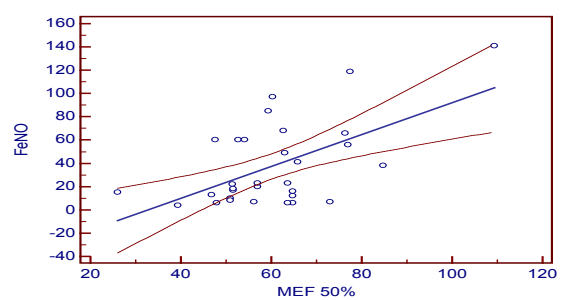

Figure 8. Correlation between of FeNO values and MEF 50 in Asthma with SMA obstruction.

y =- **44.9064 + 1.3702 x;** (r= -0.29 p=0.4) When MEF 50% increased with one unit, FENO increased with 1.37 units. Significant positive correlation.Fig. 8

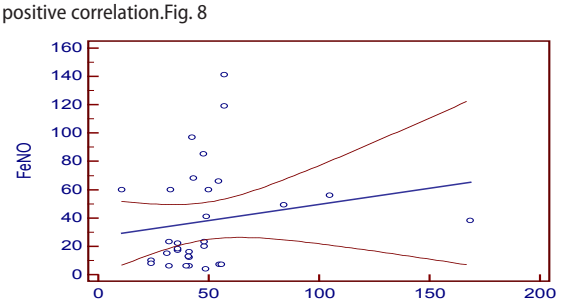

Figure 9. Correlation between of FeNO values and MEF 25 in Asthma with SMA obstruction.

y = 26.7368 + 0.2272 x (r= -0.40 p=0.3) No significant positive correlation. Fig. 9.

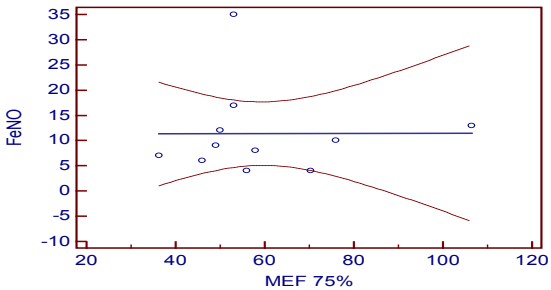

Figure 10. Correlation between of FeNO values and MEF 75 in COPD patients with SMA obstruction.

y = 11.2198 + 0.002419 x r= 0.005 p=0.9 No significant positive correlation. Fig 10.

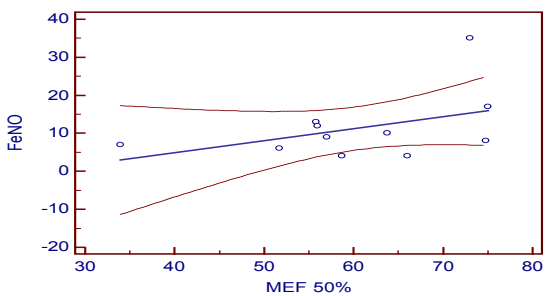

Figure 11. Correlation between FeNO values and MEF 50, in COPD with SMA obstruction.

y = -7.7003 + 0.3150 x (r= 0.4 p=0.1) No significant positive correlation. Fig.11

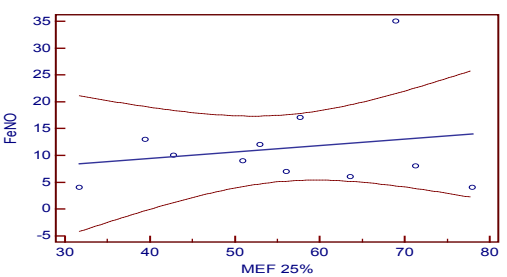

Figure 12 Correlation between of FeNO values and MEF 25 in COPD with SMA obstruction.

y = 4.6730 + 0.1199 x; r= 0.2 p=0.5 No significant pozitive correlation Fig 12.

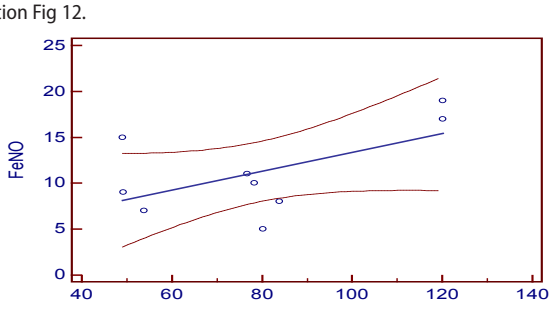

Figure 13 Correlation between of FeNO values and MEF 75 in bronchectasis with SMA obstruction

y = 3.1576 + 0.1020 x (r= 0.4 p=0.1) No significant pozitive correlation. Fig 13

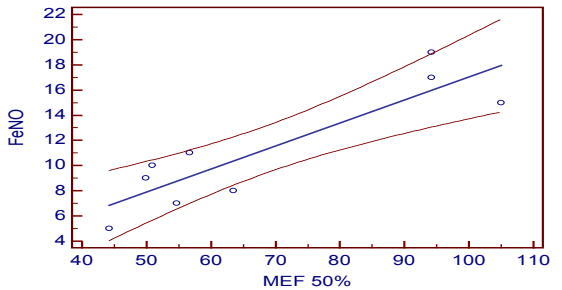

Figure 14 Correlation between FeNO values and MEF 50, in bronchectasis with SMA obstruction

y = -1.2324 + 0.1828 x p<0.01 Significant pozitive correlation. Fig 14

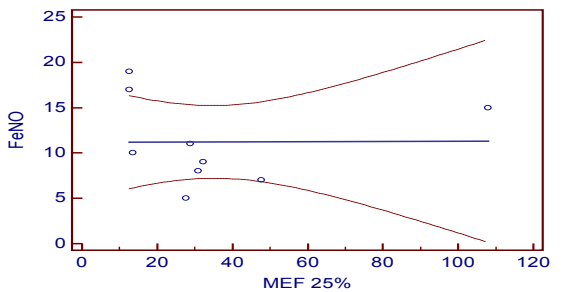

Figure 15. Correlation between of FeNO values and MEF 25 in bronchectasis with SMA obstruction.

y= 11.1716 + 0.001451 x (r= 0.1 p=0.9) No significant pozitive correlation. Fig 15

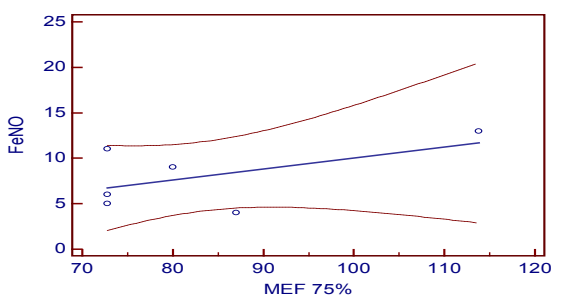

Figure 16. Correlation between of FeNO values and MEF 75 in sarcoidosis with SMA obstruction

y = -2.0576 + 0.1209 x r= 0.5 p=0.2 No significant pozitive correlation. Fig 16.

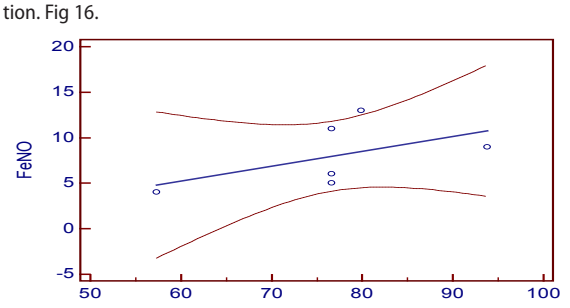

Figure 17. Correlation between FeNO values and MEF 50, in sarcoidosis with SMA obstruction

y = -4.5440 + 0.1633 x r= 0.5 p=0.2 No significant pozitive correlation. Fig 17

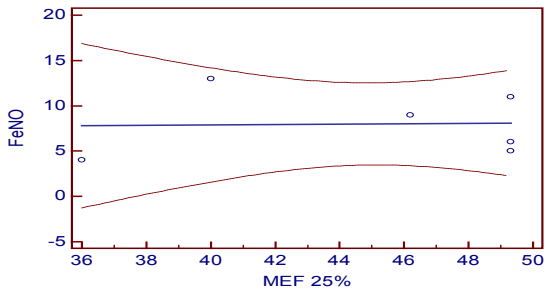

Figure 18 Correlation between of FeNO values and MEF 25 in sarcoidosis with SMA obstruction

y = 7.0052 + 0.02210 x r= 0.03 p=0.9 No significant pozitive correlation. Fig 18

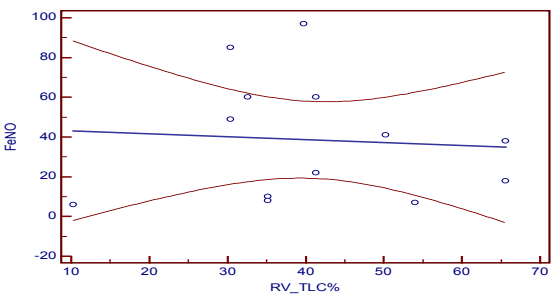

Figure 19. Correlation between FENO values and RV/TLC% in asthma with SMA obstruction

y = 44.7150 + -0.1509 x p=0.8 No significant negative correlation Fig. 19

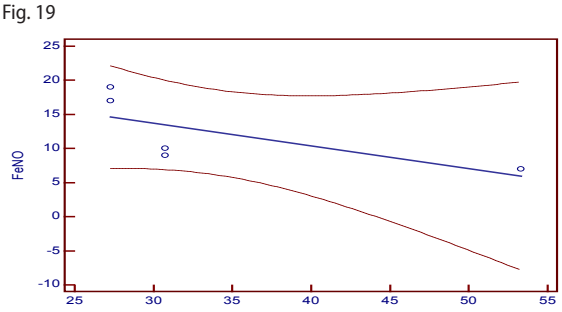

Figure 20. Correlation between FENO values and RV/TLC% in Bronchectasi with SMA obstruction

No significant negative correlation Fig 20

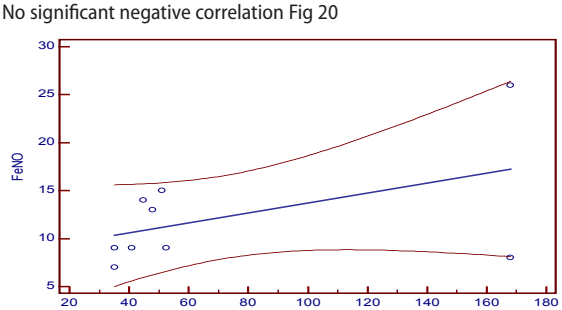

Figure 21 Correlation between FENO values and RV/TLC% in GERD with SMA obstruction

y = 8.4919 + 0.05218 x p=0.1 No significant positive correlation. Fig.21

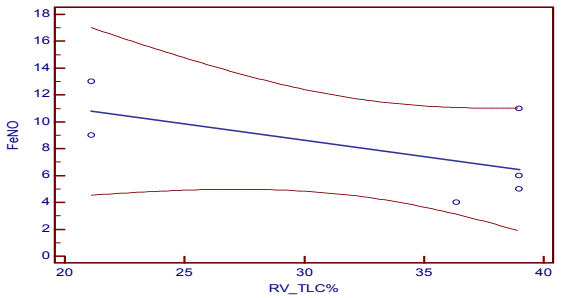

Figure 22 Correlation between FENO values and RV/TLC% in Sarcoidosis with SMA obstruction

y = 15.8751 + -0.2417 x p=0.2 No significant negative correlation. Fig.22

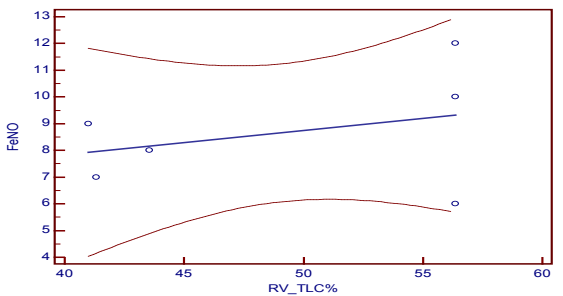

Figure 23 Correlation between FENO values and RV/TLC% in COPD with SMA obstruction

y = 4.2224 + 0.09042 x **p=0.5** When RV/TLC% increased with one unit, FENO increased with 0.09 units. No significant positive correlation Fig.23

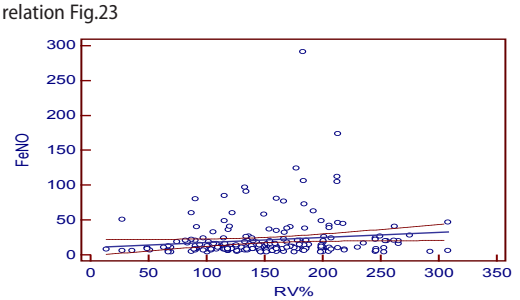

Figure 24 Correlation between FENO values and RV% in asthma with SMA obstruction

y = 10.2210 + 0.07218 x p=0.05 When RV% increased with one unit, FENO increased with 0.07 units. Significant positive correlation Fig.24

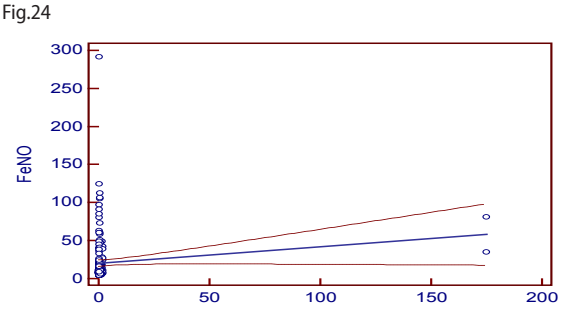

Figure 25 Correlation between FENO values and Raw% in asthma with SMA obstruction

y = 20.3492 + 0.2151 x ; p=0.06 No significant positive correlation Fig 25

CONCLUSION

FeNO is an important biomarker in assessing the etiology of respiratory symptoms .

The difference between values of FeNO in asthma and other diseases with SMA obstruction is significant. There is a positive correlation between MEF 75%, MEF 50% and FENO in asthma with SMA obstruction. There is a positive correlation between FENO and RV% in Asthma with SMA obstruction.

In Asthma with severe obstruction the FeNO values do not really represent the degree of inflammation. In bronchial small airway obstruction high values of FeNO do the diagnosis of eosinophilic inflammation. Patients with chronic cough that is not attributable to asthma, including those with cough caused by GERD, have lower NO values than patients with asthma. An elevation of exhaled NO is not specific for asthma, but an increased level may be useful in differentiating asthma from other causes of chronic cough . FENO is an important biomarker in differential diagnosis diseases associated with obstruction of the small airways.

Better and earlier identification of SMA diseases should improve the possibilities to propose earlier treatment intervention, to find the right treatment

FeNO is a promising biomarker.

"Much reasoning and few observation lead to errors, Many observation and little reasoning to truth" Alexis Carrel

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