CASE REPORT

An Interesting Case of Central and Obstructive Sleep Apnea in A Patient of Congestive Heart Failure with Unmasking of CSA's Following CPAP Use

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ABSTRACT

An elderly man with acute anterior wall myocardial infarction who underwent medical therapy followed by angioplasty and stenting was referred to our centre for evaluation of sleep-disordered breathing. The gentleman had moderate hypothyroidism for which he was on replacement therapy. At our centre PSG showed OSA for which a trial of CPAP was given. On correction of OSA by CPAP, presence of underlying CSA was unmasked. The patient improved over time on intensified medical therapy, continuous use of CPAP and regulated thyroid replacement therapy.

Keywords: OSA: Obstructive sleep apnea, CSA: Central Sleep apnea, CPAP: continuous positive airway pressure, BiPAP: bilevel positive airway pressure, PSG: polysomnography.

Introduction

Heart failure (HF) is a major risk factor for sleep related breathing disorders. Unfortunately, they remain mostly under diagnosed because of lack of awareness among primary care physicians and cardiologists. In the US, heart failure affects 1.5 – 2% of the population (1) and upto 6-10% among persons older than 65 yrs. Various studies in patients of left ventricular heart failure have shown that at least 45% have an apnea hypopnea index (AHI) of > 10/hour and 40-80% have an AHI > 15/hour. (1) Tremel et al (2) have shown that 82% of HF patients who have acute LVF had sleep disordered breathing, out of which 75% had CSA and 25% had OSA. Sin et al (3) and Javaheri et al (4) studied 450 & 81 patients and showed 72% of CSA & 33% OSA and 40% of CSA & 11% OSA respectively. However few studies have reported a higher incidence of OSA's in patients of HF. (5).

In this report we present a case of HF with OSA where presence of CSA became apparent only after institution of CPAP. The patients OSA/CSA over time were controlled with intensive medical therapy and overnight CPAP therapy.

CASE REPORT

An elderly (73 yrs) male, non-smoker, non-alchoholic patient was admitted to a city hospital in mid 2003 with acute chest pain. He was diagnosed to have acute anterior wall myocardial infarction. He was given thrombolytics (streptokinase) besides supportive care. As the patient was drowsy, complained of breathlessness and serial ABG's suggested type II respiratory failure with academia he was given a BiPAP trial. Since the patient continued to have persistent chest pain, he was taken up for coronary angiography; which showed a 80% block of the left anterior descending artery. An angioplasty with stenting was done for the blockage. ECHO studies showed concentric LVH with severe hypokinesia of apical 1/3 of inter ventricular septum, anterior wall and apical half of lateral wall. There was diastolic dysfunction with an ejection fraction of 30%. As there was little symptomatic improvement he was referred to our centre

for evaluation and further management.

The patient gave history of snoring for 2 yrs and excessive daytime sleepiness for nine months. There was history of choking/ abruptly getting up from sleep and observed pauses in breathing during sleep. There was history of nocturia and a gain in weight in the past 8-9 months. The patient was known to have HT and CAD for which he was on regular treatment for the last eight years. There was history of PSVT for which he underwent radio frequency ablation in 1996. The patient had also undergone TURP for BHP in 2002 and was on replacement therapy for hypothyroidism since March 2002.

On examination, the patient was an elderly man with a pulse of 100/min, RR 22/min & BP on supine position of 140/80 mmHg. He had a height of 160 cm and a weight of 83 Kg (BMI: 32 Kg/Ht^2). His neck circumference was 43 cm and corrected neck circumference 50 cm (correction factor + 4 cm for hypertension and +3 cm for snoring (6). His CVP was raised and he had bilateral pitting edema of the feet. Examination of the chest was normal except for bilateral inter and infra scapular inspiratory crackles. Examination of CVS and abdomen was essentially normal. Examination of the CNS revealed a slow relaxation of deep tendon reflexes.

An ENT examination revealed a grade II tongue, thick, low palate; tonsillor bulk grade II; posterior pillars were splayed wide with inter pillar distance of < 20 mm. The uvula was > 10 mm and edematous. The nose showed evidence of B/L chronic hypertrophic changes. The larynx was normal. (7)

On investigation his haemogram, routine urine examination, serum biochemistry, electrolytes and lipid profile were normal. The thyroid function test was deranged (free T3: 0.42 pg/ml (1.42-4.2), Free T4: < .15ng/dl (0.8-2.0); and TSH: > 40 1u/ml (.25-5.0). His X ray chest was normal. ECG showed evidence of old anterior wall MI. The PFT showed a mild obstructive ventilatory defect (FVC-1.72L 57%; FEV1: 1.27 L (55%); FEV1/FVC: 73.7%; FEF: 25-75; 0.82 L: 38% and SVC: 2.13 L (71%). Serial ABG's at this stage showed hypoxemia with mild hypocapnia. A repeat ECHO revealed findings similar to the previous study with an EF of 33%. Despite intensive medical therapy with diuretics, ACE inhibitors, oxygen and theophyllin, there was no improvement in clinical features and hypoxemia, therefore, the patient was taken up for split night polysomnography.

The PSG showed evidence of severe obstructive sleep apnea with an AHI index of 60 /hr. There was severe degree of oxygen desaturation with the lowest recorded SaO_2 of 78%, associated with snoring.

The patient was put on CPAP and pressure was gradually increased to 15 cm H_2O, resulting in complete elimination of obstructive apneas, snoring and oxygen desaturation. Immediately after correction of the obstructive apneas the patient started showing episodes of periodic breathing with variable periods of central apneas. Initially it was thought that the central apneas could be the result of high CPAP pressure. However, with repeated adjustment of CPAP pressures and using the minimum pressure, which resulted in abolition of obstructive apneas the periodic breathing continued. Keeping in view the patients background of ischemic heart disease with HF and an EF of 33% it was presumed that the periodic breathing were due to cardiac failure which were being masked by the obstructive apneas. (Fig 1 to 4).

After institution of CPAP for sleep disordered breathing and intensified medical therapy for HF, the patient's thyroid replacement therapy was stepped up. Follow up after three months showed normalization of thyroid functions and control of SDB on CPAP.

DISCUSSION

Heart failure (HF) affects 5-6 million North Americans and is increasing in prevalence. (8) In India heart disorders including coronary artery disease have attained epidemic proportions. Various pharmacological agents have had little effect in hospitalization & death rates (8). Therefore, there is a need to develop newer, widely acceptable and cost effective approaches to the therapy of HF.

An important limitation to the current guidelines for evaluation and management of chronic HF is their focus on the patient as he/she presents while awake.(9) This presupposes that the mechanisms that contribute to the pathophysiology or progression of HF are quiescent during sleep. Sleep normally is a time for cardiac relaxation, however, about 50% of HF patients have OSA & CSA both of which disrupt the normal relaxing effects of sleep on the cardio vascular system and may actually worsen HF.

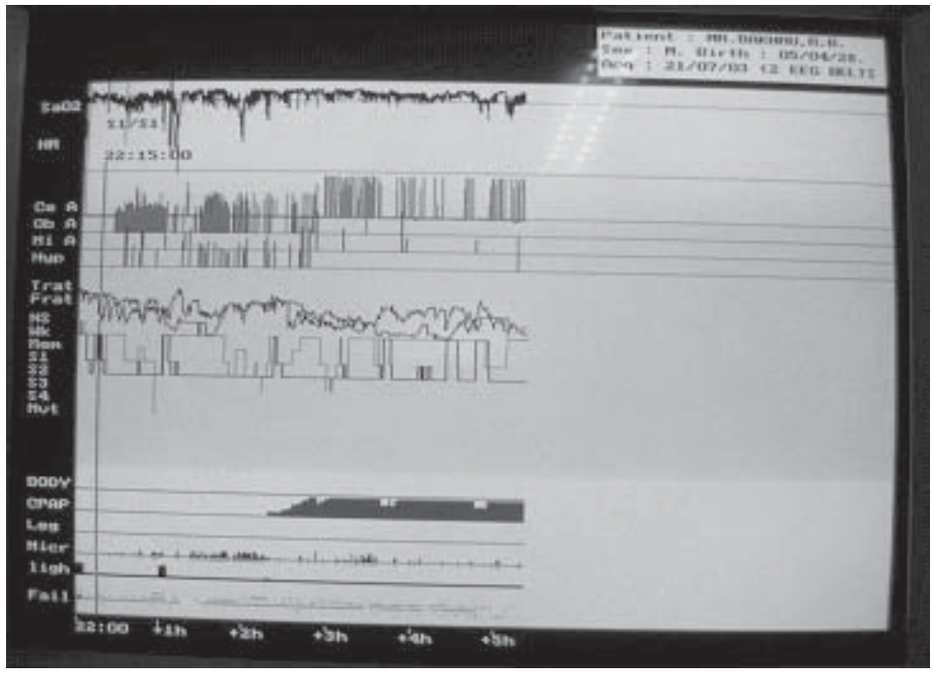

Fig 1: Whole night histogram of patient showing initial predominant OSA which after CPAP exposed underlying CSA, with improvement in saturation and snoring.

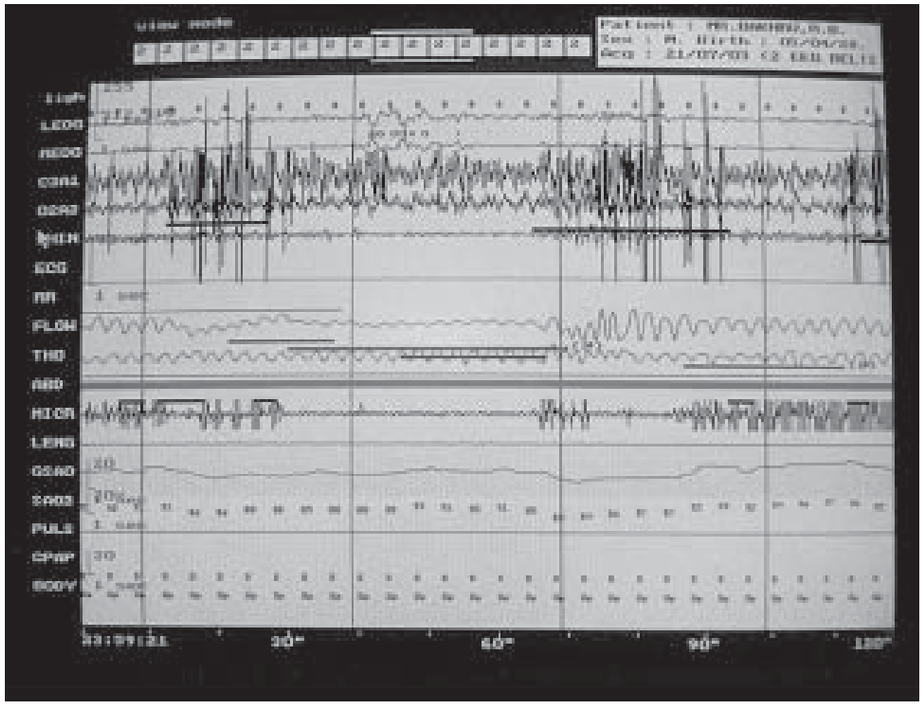

Fig 2: PSG of patient before application of CPAP showing an episode of OSA with snoring and desaturation

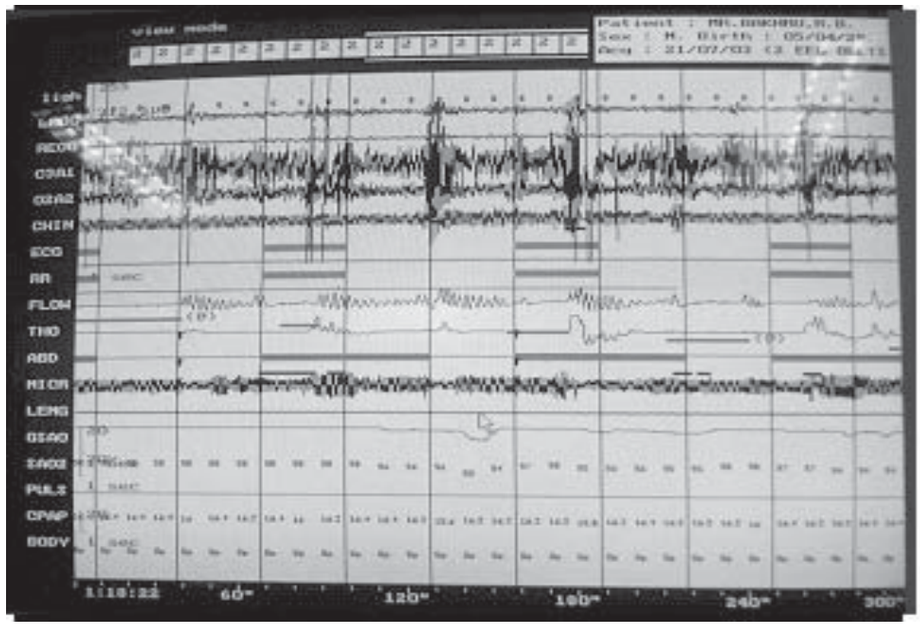

Fig 3: PSG of patient depicting presence of Cheyne Stokes respiration after institution of CPAP

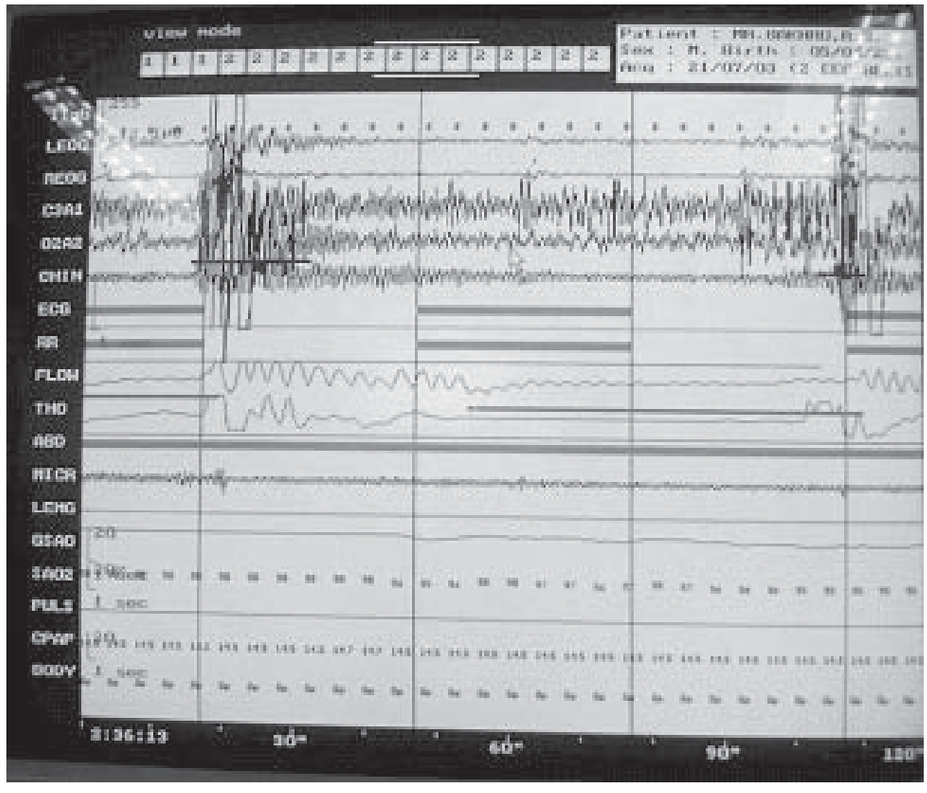

Fig 4: PSG of patient after institution of CPAP at a pressure of 14.5 cm H_2O; showing periodic breathing (central sleep apneas).

Looking at the risk factors, for OSA and CSA Javaheri et al (4) found OSA patients had significantly higher body weight (112 ± 30 versus 75 ± 16 Kg) and prevalence of habitual snoring (78% versus 28%). However episodes of apnea and hypopneas (36 ± 10 versus 47 ± 21), episode of arousal (20 ± 14 versus 23 ± 16) and desaturation (lowest saturation, 72 ± 11% versus 78 ± 12%) were similar in the different types of apnea. Sin et al (3) found risk factors for CSA were male gender (odds ratio (OR) 3.50; 95% confidence internal [CI] 1.39 to 8.84), atrial fibrillation (OR 4.13; 95% CI 1.53 to 11.14), age > 60 yrs (OR 2.37; 95% CI 1.35 to 4.15), and hypocapnia (PCO_2 < 38 mm Hg during wakefulness) (OR 4.33; 95% CI 2.50 to 7.52). Risk factors for OSA differed by gender: in men, only body mass index (BMI) was significantly associated with OSA (OR for BMI > 35 Kg/ht^2 6.10; 95% CI 2.86 to 13.00); whereas in women age was the only important risk factor (OR for age > 60 yr, 6.04; 95% CI 1.75 to 20.0). Our patient being about 73yrs, BMI of 35 Kg/ht^2, male gender, with arterial PCO_2 of about 38 mmHg (awake) had most characteristics associated with SDB in HF.

The pathophysiology of OSA & CSA is dissimilar. Obstructive sleep apneas are caused by collapse of the pharynx in sleep. In patients of OSA the pharynx is narrowed and highly compliant. In this setting the superimposition of the normal withdrawal of pharyngeal dilator muscle tone at sleep onset causes the pharynx to occlude, triggering apnea. (10) Obesity is the chief risk factor, because of layering of fat adjacent to the pharynx narrows its lumen. (11) Withdrawal of pharyngeal muscle tone during CSR (12) and shift of edema fluid (13) are also attributed as additional risk factors.

HF patients with CSA hyperventilate chronically due to stimulation of pulmonary vagal irritant receptors by pulmonary congestion. (14). This increases when the patient lies flat due to increased venous return producing hyperventilation and reduction in $PaCO_2$ below the threshold for ventilation, triggering a central apnea.(15) followed by arousals (16). CSA's are sustained by recurrent arousals resulting from apnea induced hypoxia and the increased effort to breathe during the ventilatory phase because of pulmonary congestion and reduced lung compliance. The length of the ventilatory phase is inversely proportional to cardiac output, reflecting a delayed transmission of changes in arterial blood gas tension from the lung to the chemoreceptors(17). This was first demonstrated by Klein (18) and later by Pryor (19) in their studies. The above, along with large negative swing in intrathoracic pressure occurring in the hypercapnic phase of periodic breathing, adversely affect various cardiovascular functions and are potentially detrimental in presence of systolic and diastolic dysfunction and coronary artery disease.(20),(21) The effect of HF on OSA & CSA, its pathophysiological aspects, clinical features and therapeutic options has been reviewed by Bradley & Floras (8) (22) in their articles on the subject.

Clinical features of patients with HF and OSA are similar to those of OSA patients without HF. The patients being usually obese and have history of loud habitual snoring. Among patients with HF with CSA there are no disease specific symptoms. Patients who are awake during peak of ventilation after apnea may report paroxysmal nocturnal dyspnea (23). Although there is sleep fragmentation, only few patients of OSA or CSA (4) among patients of HF complain of excessive day time sleepiness and therefore many of them remain occult (24). Our patient however presented with a long history of snoring and EDS.

In some patients of HF, CSA and OSA coexist as seen in our patient. Tkacova et al (25) noted a gradual shift from predominantly obstructive apneas at the beginning of the night to predominantly central apneas towards the end in such cases. They evaluated this by studying minute ventilation, transcutaneous PCO_2, circulation time and periodic breathing cycle length during overnight PSG in 12 patients of CHF. They concluded that overnight shift from OSA to CSA is related to reduction in $PaCO_2$ caused by increases in minute ventilation. Most importantly, the close relationship between overnight reduction in PCO_2 and increase in circulatory delay suggests that the overnight shift in apnea type is linked to deterioration in cardiac function. Hall et al (26) have also noted that this lung to chemo receptor circulatory delay owing to low cardiac output, and cycle length of periodic breathing are longer in CHF patients with sleep apnea than in patients with sleep apnea but normal cardiac function. This concept is consistent with the suggestion of Somers (27) that hemodynamic instability in patients with CHF may be related to instability in apnea type as well. Solin et al (14) demonstrated that $PaCO_2$ is inversely related to the capillary wedge pressure in patients of CHF and frequency of CSA is directly related to the left ventricular filling pressure. Periodic breathing cycle length and lung to ear circulation time (LECT) are proportional to cardiac output suggestive of nightly fall in cardiac output were

also shown by Hall et al (26) & Tkocava et al (28). These studies raises the possibility that over months or years the presence of OSA could predispose HF patients to CSA which has more ominous implications.

Another confounding factor in our patient was the presence of hypothyroidism, where OSA is thought to occur due to deposition of mucopolysaccharides and protein extravasation into the tissues of the pharynx & tongue (29). Other hypothesis suggested is abnormalities in ventilatory control during sleep (30) and blunted response to hypoxia (31). Central sleep apneas have been noted in hypothyroidism(32). The contribution of hypothyroidism in our patient to the CSA/OSAs cannot be commented on as the patient was also on CPAP during the follow up phase besides medical therapy for HF and regulated thyroid replacement therapy.

Though general therapeutic measures like weight reduction, abstinence from alcohol and sedatives (33) may reduce the severity of OSA, (34) CPAP remains the corner stone of therapy in OSA whether associated with or without HF. CPAP via nasal mask alleviates OSA, improves sleep quality, reduces daytime sleepiness, augments neurocognitive function, and may lower nocturnal and daytime blood pressure (35,36). Regular CPAP use has also been demonstrated to increase the ejection fraction and improve dyspnea(37) in HF. There is no evidence that pharmacological agents used to treat HF have any influence on the severity of OSA(38).

Treatment of central sleep apnea may be achieved in several ways (23,39). Javaheri in a recent review has discussed all aspects related to treatment of central sleep apnea in HF (20). The principal reason for treating CSA is the potential to improve cardiovascular function, quality of life and longevity (40,41). Because CSA is a manifestation of advanced HF, the first consideration is to optimize drug therapy. Amongst these measures aggressive diuresis, angiotensin converting enzyme inhibitors and B blockers form the corner stone (13). Theophyllin also plays a role as a respiratory stimulant by competing with adenosine at some receptor sites. In the CNS theophyllin stimulates respiration by competitive inhibition of adenosine (42). Another drug helpful in treatment of CSA in HF is acetazolamide a carbonic anhydrase inhibitor that produce metabolic acidosis thereby stimulating the peripheral and central chemo receptors (43,44). Supplemental nasal oxygen administered during sleep is a potent therapy for CSA in systolic heart failure (45,46). Several studies (47,48) have shown that apnea- hypopnea index decreases with oxygen inhalation. Randomized, placebo controlled double blind study has also shown that exercise capacity improves within a week of oxygen (49). This occurs perhaps, due to a reduction in ventilatory response to CO_2 following a rise in $PaCO_2$ (50). Also, oxygen reduces sympathetic activity (51) and urinary non-epinephrine excretion (52). Although inhalation of CO_2 suppresses CSA, this has little or no therapeutic role (53,54).

If the above measures fail other non-pharmacological measures have to be resorted to. The chief therapeutic options here are various forms of non-invasive positive pressure ventilation including CPAP, BiPAP and adaptive pressure support servo ventilation, all of which alleviate CSA over a period of time (41,55). However, thus far, the only intervention whose effects on cardiovascular outcomes have been evaluated is CPAP. CPAP helps by decreasing left ventricular after load (56), augments stroke volume (57), reduces cardiac sympathetic activity (58), decreases right and left ventricular end diastolic volume (59), ventricular ectopic beats (60), improves ejection fraction and improves quality of life (61,62).

Bradley et al (63) in the CANPAP trail have shown in 250 patients that although there was decrease the AHI's, nor epinephrine levels, improvement in mean O_2 saturation, ejection fraction and six minute walk test; there was no difference in the event rates i.e. death and heart transplantation. Although improvement in cardiac function has been shown in patients in CSA with and without CSR, mortality advantage was only seen in patients of CSA with CSR (64). Even without CPAP, presence of CSR with CSA increases mortality in patients with CHF (65). Our case showed that with intensified medical therapy and CPAP use there was improvement of OSA' s and over time resulted in significant improvement in frequency of CSA, improvement in oxygen saturation and cardiac function (EF).

Other treatment modalities like cardiac transplantation usually eliminate central sleep apneas (66,67). Another mode of therapy found useful in patients with mild left ventricular systolic dysfunction with CSA is atrial overdrive pacing (68).

In conclusion, our case depicts the presence of both OSA and CSA in a patient of severe HF with unmasking of CSA following CPAP use. Further with continued use of overnight CPAP, intensive medical therapy for HF and regulated thyroid replacement therapy follow up PSG (after three months) demonstrated subjective

and objective (ABG & PSG) improvement with significant reduction in periodic breathing.

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