ON-LINE DOCUMENTS:

3 CME cases

Patient fact sheet

CME Case 1

Medical history

Mister O is a 68 years old man, who used to run a local restaurant. He is consulting the outpatient respiratory clinic because of COPD. His medical history consists of: hypertension (1989), myocardial infarction (1992), coronary artery bypass graft (1999), depression (1999), chronic lower back pain (2002) and obstructive sleep apnea (2009). He tells his physician he is increasingly impaired during walking because of dyspnea. It is very difficult for him the reach the shopping centre, which is located at 500 metres from his home. Stair climbing is also very difficult; sometimes he actually sleeps in his living room during the night. He has very little cough and almost no sputum. However, when he is speaking a lot and after exercise, he has episodes of cough. In the last year, he did not receive any course of oral corticosteroids or antibiotics because of an exacerbation of his COPD. He smokes about 20 cigarettes per day and has acquired 55 packyears. In the last year he gained about 10 kilograms of weight. He is not very physically active. Medication: long-acting muscarinic antagonist, long-acting beta2-agonist, diuretic, angiotensin receptor blocker, anti-aggregate, selective beta-blocker, antilipaemic. Body composition and lung function of mister O are presented in table 1. Also laboratory examination was performed (table 2).

Table 1. Body composition and lung function

Body composition				
Height	cm	176.5		
Weight	kg	118.5		
BMI	kg/m^2	38.0		
FFM	kg	71.9		
FFMI	kg/m^2	23.1		
T-score	L2-L4	-1.5		
T-score	hip	-1.5		
Lung function				
FEV_1	l (%predicted)		1.98	(66.1)
FVC	l (%predicted)		4.01	(95.4)
FEV_1/FVC	%		46.8	
FRC	l (%predicted)		3.40	(92.9)
RV	l (%predicted)		2.64	(101.7)
TLC	l (%predicted)		6.87	(97.8)
RV/TLC	%		38.4	
DLCO	mmol/min/kPa (%predicted)		4.49	(49.7)
KCO	mmol/min/kPa/L (%predicted)		0.89	(69.1)

Table 2. Laboratory results.

Hemoglobin,	mmol/l	9.1	
Leukocytes	109/l	8.8	
CRP	mg/l1	2.47	
Creatinine	umol/l	121	
Glucose	mmol/l		7.7
Cholesterol	mmol/l	4.6	
LDL	mmol/l	2.90	
Triglycerides	mmol/l	1.65	

Question 1) What is your interpretation of the medical history, given the data in tables 1 and 2.

Answer:
This is a 68 years old man with COPD GOLD 2, mMRC 2, no frequent exacerbations or hospitalisations. He is obese, has a preserved fat-free mass but a somewhat reduced bone mineral density. In addition, he has significant cardiovascular, skeletomuscular and psychological comorbidity. He is in GOLD group B. The main risk factor for disease progression is still present: smoking.
The lung function shows moderate airflow limitation. Instead of static hyperinflation, which could be anticipated based on his COPD, there is a tendency towards lower lung volumes as indicated by the somewhat lower functional residual capacity, while residual volume and total lung capacity are as predicted and RV/TLC is increased. This is a typical lung function for obese subjects, resulting from reduced lung compliance [1]. Also in patients with COPD, FRC is decreased in obese compared to normal weight patients [2]. Diffusion capacity of this patient is moderately reduced. This cannot be attributed to obesity, as lung carbon monoxide transfer factor (DLCO) is in the normal range or increased in obesity [3]. In combination with chronic airflow limitation, this suggests that the patient has some degree of pulmonary emphysema. Laboratory results indicate glucose intolerance as a newly diagnosed comorbidity [4].

Because of a discrepancy between the degree of airflow limitation and symptoms and the progressive nature of the subjective exercise intolerance, the respiratory physician decides to assess the exercise capacity and muscle function of the patient. Results are presented in table 3.

Table 3. Exercise tests and muscle function

Peak cycle ergometry				
Wmax	W (%predicted)	67	(38)	
VO2max,	ml/min (%predicted)	997	(42)	
RER max		1.12		
VEmax,	l/min (%predicted)		42	(79)
Heart rate	beats/min (%predicted)	72	(47)	
Saturation	% before - after	95 - 96		
BORG dyspnea	before - after	0 - 5		
BORG fatigue	before - after	0 - 10		
6MWT				
Distance	m (%predicted)	253	(42)	
Saturation	% before – after	95 - 94		
Quadriceps muscle strength				
Peak torque	Nm (%predicted)	169	(70)	

Question 2) Interpret the results of these tests regarding the clinical diagnosis and comorbidities of this patient.

Answer:
Peak exercise capacity is severely reduced. RER suggests that the patient did a maximal effort, although both ventilatory and cardiocirculatory limits were not reached. However, it should be kept in mind that the patient used beta-blockers. No desaturation occurred. Results of this peak cycle ergometry suggest that the patient is severely deconditioned. Six-minute walking distance is also severely impaired, without desaturation. Despite the preserved fat-free mass, the patient has a moderate impairment in muscle function.

Based on the assessment of the integrated health status, mister O is referred for a pulmonary rehabilitation program by his respiratory physician.

Question 3) Which would be your treatment goals for a pulmonary rehabilitation program for this patient?

Answer:
Quit smoking, reconditioning, cardiovascular risk reduction by aerobic exercise training and some weight loss, adaptation towards more healthy lifestyle

Question 4) What would be the ideal pulmonary rehabilitation program for this patient?

Answer:
No specific pulmonary rehabilitation programs have been developed for obese COPD patients. Several studies indicated that non-weight bearing exercise capacity (cycling) is relatively preserved [2] in comparison with weight bearing exercise performance (walking) in obese patients [5]. However, it is currently unknown which training modality is more effective in these patients. A recent study indicated that water-based exercise training may be more effective in obese COPD patients compared to land-based exercise training [6]. The impact of comorbidities on the outcomes of pulmonary rehabilitation remains to be established [7].

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3. Collard P, Wilputte JY, Aubert G, et al. The single-breath diffusing capacity for carbon monoxide in obstructive sleep apnea and obesity. Chest 1996;110:1189-93.
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CME Case 2

IC is a 69 year old male, retired mechanic. He initially presented to his GP with breathlessness on exertion five years ago and was diagnosed at that time with COPD. There is no history of respiratory illness as a child or earlier in adult life. He successfully gave up smoking 12 months ago but has a 54 packyear history.

Currently he is breathless on walking a few minutes on the flat (MRC score 4). He experiences 3-4 exacerbations annually which are treated with courses of prednisolone and antibiotics which he keeps at home. He has had one admission to hospital 12 months previously.

There are no significant comorbidities and no progressive weight loss.

He does not use home oxygen. Medications are:

Fluticasone 500 mcg + Salmeterol 50 mcg - 1 puff bd
Tiotropium handihaler - 1 puff od
Salbutamol - 2 puffs as needed

He has not attended pulmonary rehabilitation.

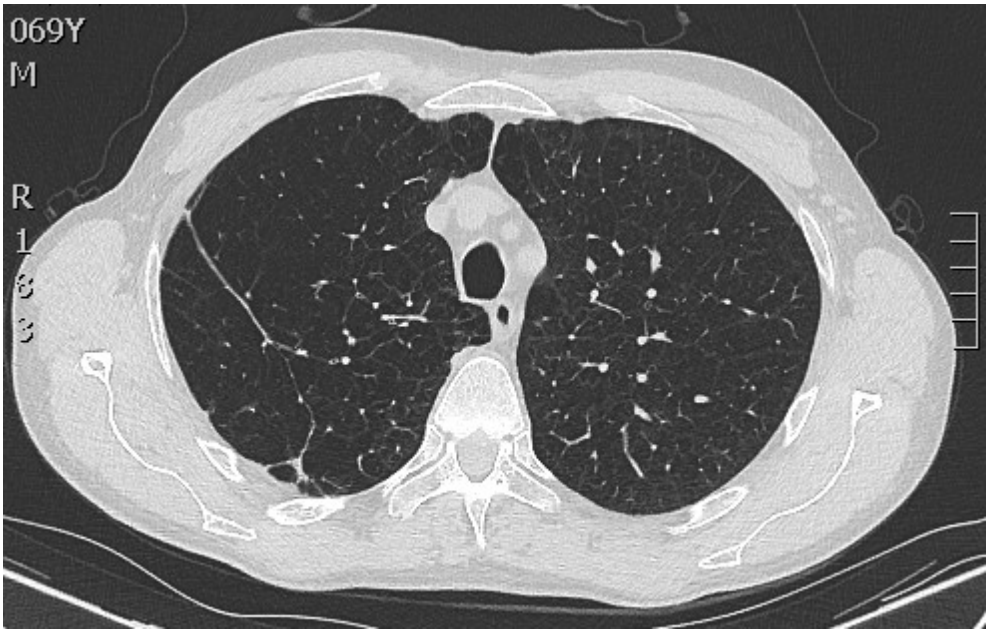
On examination there was evidence of pulmonary hyperinflation with reduced breath sounds in keeping with emphysema. There was no clinical evidence of cyanosis, anaemia, cardiac failure or oedema.

<u>Assessments/Investigations:</u>

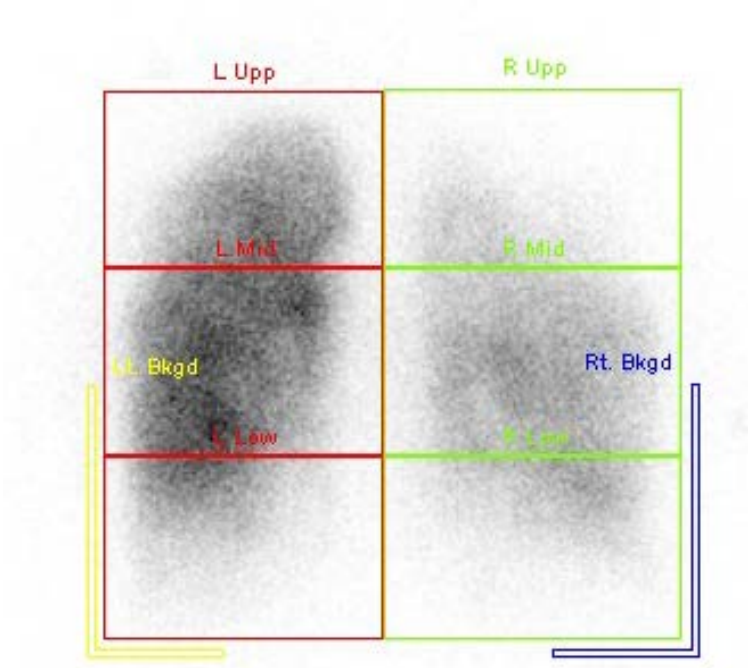
Lung Function:	FEV_1:	0.82L (28% predicted)
	FVC;	2.99L
	FEV_1/FVC Ratio	37%
	Residual Volume	258% predicted
	RV/TLC ratio	68%
	TLCO	41% predicted
	KCO	52% predicted
CAT score:	21	
BMI:		21 Kg/m^2
DEXA:	FFMI:	15.3 Kg/m^2
	SMI:	6.27Kg/m^2
	Bone Min Density:	T score: -2.0
Exercise Performance:	ISWT:	140m
	SaO_2 rest:	95%
	SaO_2 post exercise:	88%
	QMVC:	19.1Kg (48% predicted)

<u>Imaging:</u>

The High Resolution CT scan below shows heterogeneously distributed emphysema with upper lobe predominance. Minor bronchiectasis was observed in the lower lobes.



The perfusion scan below shows reduced perfusion in the Right upper lobe.



Questions:

1. How would you assess the severity of disease and nutritional risk in this patient?

2. What management options would you consider?

Interpretation:

He has severe COPD GOLD 3/D. The burden of disease is substantial because he has severely impaired exercise performance, muscle strength and health status (CAT score 21/40) and is experiencing frequent exacerbations. He is underweight by both BMI and body composition criteria, but there is no progressive weight loss. He meets the criteria for sarcopenia (SMI < 7.23 kg/m^2). Using the risk stratification diagram in the document he would fall into the box second from top and second from left (low-moderate mortality risk). He has osteopenia but not established osteoporosis (T score -2.0).

Management options:

Impaired performance:

1. Refer for pulmonary rehabilitation. He will benefit from both resistance and aerobic training (reduced muscle strength and reduced aerobic capacity).
2. Consider Lung volume reduction therapies as he has severe pulmonary hyperinflation and heterogeneously distributed emphysema with a target area in the right upper lobe. VATS LVRS or endobronchial valve therapies are options.
3. Assess for ambulatory oxygen as he desaturates during exercise.

Impaired body composition:

1. Dietician referral to provide advice on nutritional intake and consider nutritional supplementation ideally in conjunction with pulmonary rehabilitation as above.
2. Screen for hypogonadism as increased prevalence in underweight patients with COPD.
3. Recommend weight bearing exercise and ensure adequate dietary calcium intake to maintain bone mineral density. Consider monitoring bone mineral density with DEXA.

Frequent Exacerbations:

1. Recommend annual influenza vaccination
2. Screen sputum for bacteriology.
3. Refer for chest physiotherapy and consider mucolytic if sputum production excessive.
4. Consider antibiotic prophylaxis with low dose macrolides if high exacerbation frequency continues.

CME Case 3

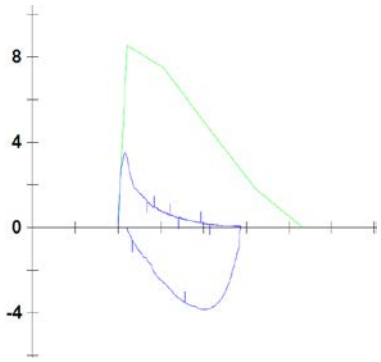
Clinical scenario

A 68 old man with smoking history of 45 packyears is referred to the outpatient clinic with increasing difficulties of breathing at exertion for more than five years. Complaints initially occurred with strenuous cycling but since a hospital admission for acute diverticulitis, also appeared during milder physical activities such as climbing stairs and gardening. Because of increasing symptoms and also because of the orthopaedic problems of his wife, the couple decided to move from the countryside to an apartment in the city 2 years from now.

At that time, the diagnosis of COPD was established by a general practitioner based on a pulmonary function (FVC: 3.9L (95% predicted), FEV_1: 2.2L (66% predicted)). Inhalation therapy with a once daily long-acting anticholinergic drug was started resulting in little symptomatic relief. One year later, the patient experienced a first acute exacerbation for which oral steroids and antibiotics were given. Tapering down systemic steroids was associated with the reoccurrence of symptoms, reason why the patient was still on low dose of methylprednisolone for more than 4 months at the moment of presentation. He is currently complaining of dyspnea at daily activities such as dressing and washing. Further anamnesis points to a weight loss of more than 10 kg over the last year despite normal appetite. There is also intermittent pain in the back, especially when coughing. The patient is anxious about the future and feels guilty when discussing his persistent smoking behaviour.

Clinical exam reveals hyperinflation, silenced vesicular breathing, a prolonged expiration and mild expiratory wheezing. There are no clinical signs of cardiac congestion. The upper part of the thoracic vertebral column has a painful palpation. Breathing rate 14/min, pulse rate 75/min, blood pressure: 145/90 mmHg. Body weight: 58 kg, Body mass index: 20 kg/m^2
Further clinical examination of heart, neck, lymph node regions and abdomen is normal

I. A complete pulmonary function gives the following results:



FVC:	2.8 L (68% predicted)
FEV_1:	1.17 L (38% predicted)
TGV:	4.4 L (130% predicted)
RV:	3.4 L (140% predicted
TLC:	5.8 L (79% predicted)

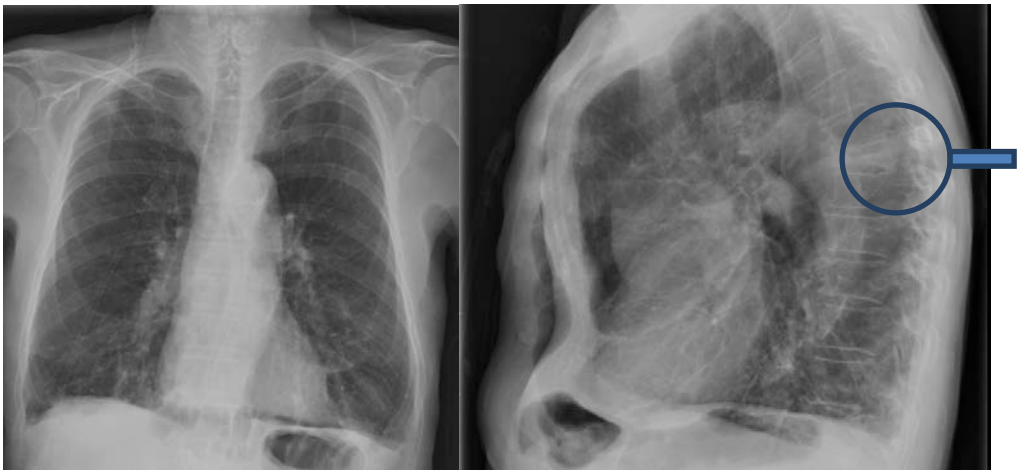
Which of the following diagnoses is part of your differential diagnosis?

1. An acute COPD exacerbation
2. Disease progression
3. Pneumonia
4. Lung cancer
5. Pulmonary embolism
6. Pulmonary cachexia and steroid induced myopathy

Answer:

Despite the rapid deterioration of pulmonary function, there are no clinical signs of an acute COPD exacerbation or pneumonia at the moment of presentation. There is no respiratory distress at rest neither increased sputum production, purulence or fever. Pulmonary embolism may be a reason for unexplained dyspnea but is unlikely given the chronic history and the documented drop of pulmonary function. As total lung capacity (TLC) is unexpectedly low and because the decline of FVC and FEV_1 is far beyond the expected rate of decline, other factors than regular disease progression with increased air trapping should be explored. In light of the involuntary weight loss (cachexia), the pain over the vertebral column and the high risk profile, lung cancer with atelectasis should be excluded. An alternative reason for the drop in pulmonary function might be vertebral impaction or severe respiratory muscle weakness with a reduction of TLC and subsequently smaller dynamic volumes.

II. X ray, ECG and blood biochemistry are taken.



Blood biochemistry and ECG are within the normal ranges. X-ray of the chest confirms hyperinflation with flattening of the diaphragm, and excludes heart failure and atelectasis as the primary cause of drop in pulmonary function. Lateral X-ray demonstrates a vertebral compression fracture of the dorsal vertebral corpus (D5) with considerable height loss

What are the other tests that you would consider in this casus?

1. DEXA scan

2. Peripheral skeletal muscle force
3. Respiratory muscle force
4. CT scan
5. All of them

Answer.

We think that all tests are of value in the further differentiation of the medical problem. A CT scan of the chest may still be considered to exclude a small cancer lesion with vertebral metastasis. More likely is the diagnosis of steroid and COPD related osteoporosis associated with skeletal muscle wasting and cachexia. Although the drop in FEV_1 can be attributed to increased airway obstruction, the restrictive component due to vertebral collapse will also result in smaller spirometric volumes. Loss of inspiratory muscle strength may be an additional factor to explain the reduced inspiratory capacity. DEXA scan is needed to confirm the diagnosis of osteoporosis and to monitor its treatment. It also allows quantification of body composition and fat free mass. As indicated by the risk assessment figure (figure 1 in statement), a BMI of 20 and the involuntary weight loss of more than 10 kg (15% of total body weight) are associated with impaired prognosis and a high risk of mortality. Skeletal and respiratory muscle function may further document the urgent need of multidisciplinary intervention.

III. DEXA scan confirms the diagnosis of osteoporosis of the femur and vertebral column (both T scores < -2.5). DEXA determined FFM is 45kg resulting in FFMI of 15.5 kg/m^2. Skeletal muscle wasting and subsequent weakness is confirmed by a quadriceps isometric strength of 52 Nm (40% predicted) and a maximal inspiratory pressure (MIP) of -5.5 kPa (50% predicted).

What is the multidisciplinary intervention you would recommend?

1. Smoking cessation, nutritional intervention
2. Optimisation of medical therapy and smoking cessation
3. Training, nutritional intervention and smoking cessation
4. Optimisation of medical therapy, nutritional intervention, smoking cessation and training

Answer

The final diagnosis is COPD GOLD D (mMRC 4, 2 exacerbations, FEV_1 < 50%pred). The rapid clinical deterioration might be explained by the accumulation of negative factors such as inactivity, persistent smoking, repeated exacerbations, and frequent use of systemic steroids. With the secondary development of cachexia, osteoporosis and muscle wasting, the risk of major events and mortality is high. The prognosis is poor but multidisciplinary intervention is warranted in an attempt to reverse the high risk situation and to improve symptom control, exercise tolerance and quality of life. Optimal medical therapy includes maximal bronchodilation and inhaled corticosteroids because of frequent exacerbations. LABA-ICS combination therapy is added to once daily LAMA. The deleterious maintenance treatment with systemic steroids should be tapered down and completely abandoned. Osteoporosis is treated with bisphosphonates in combination with calcium and vitamin D supplementation. The patient is referred for rehabilitation to a specialised centre. The program will consist of aerobic interval training combined with strength exercises. Special attention will go to back saving exercises. Nutritional intervention will focus on a healthy diet with sufficient caloric intake, and if needed, carbohydrate and protein rich supplements will be added on top of regular meals. Within the context of this multilevel approach, any attempt for smoking cessation will become more successful.

Patient fact sheet

Diet, Nutrition and Chronic Obstructive Pulmonary Disease - COPD

COPD results from complex interactions between genes and environment. Regarding the latter, increasing attention has been given to the weight of environmental factors, such as physical inactivity, air pollution, smoking and diet. There is now a large body of evidence supporting the role of diet in the natural history of COPD, as well as the health value of certain nutritional interventions, for example, in the context of pulmonary rehabilitation.

Diet surveys and, more recently, dietary habits analyseis of dietary habits have shown that in addition to abnormal overall calorie intake, the intake of individual nutrients and certain dietary behaviours can have protective or harmful effects. The main risk factor for COPD in the developed world is cigarette smoking, but up to one-third of patients with COPD (especially in developing countries) have never smoked, implying that other factors are also important.

In large studies in general populations in the USA, it was reported that a high intake of a "prudent" dietary pattern (e.g. fruit, vegetables, fish, and whole-grain products) decreased the risk of newly diagnosed COPD, whereas a high intake of a Western-type pattern increased this risk. More recently, it has been reported that "traditional" dietary habits (with high intake of red meat, processed meat, boiled vegetables, added fat, coffee, beer, and potatoes, but reduced consumption of soy products, low-fat dairy products, tea, breakfast cereal, brown rice, pizza, juice and fruit) was associated with reduced lung function and a higher prevalence of COPD. A high intake of refined foods was associated with an accelerated decline in lung function over 5 years. In relation to specific foods, special attention has been paid to fibre intake. It has been consistently reported that dietary fibre intake has independent inverse associations with the incidence and symptoms of COPD and with decline in lung function. In addition to foods and nutrients with potential beneficial effects, several studies have focused on those with potential harmful effects. Two studies have reported associations between frequent or high consumption of cured meats and the risk of developing COPD. A recent study has extended this association to include the evolution of the disease, revealing that high cured meat consumption is linked to a higher risk of readmission to hospital with COPD.

The following dietary guidelines are drawn from recommendations by the World Health Organization (WHO)WHO, the European Food Safety Authority (EFSA), the European Respiratory Society (ERS), the American Thoracic Society (ATS) and the Société de Pneumologie de Langue Française (SPLF). Eating foods rich in antioxidants can counter the damage done to the body by oxidative stress, as antioxidants effectively "mop up" free radicals and so prevent them from causing damage. Sources of vitamin C include citrus fruits (oranges, lemons, grapefruit), kiwi fruit, broccoli and green peppers; beta-carotene is present in apricots, mango, carrots, peppers and spinach; vitamin E can be found in grains, wheat germ, almonds and peanuts; lycopene is found in tomatoes and processed tomato products; and grains, Brazil nuts, animal products (especially organ meats) and seafood contain selenium. Magnesium is the fourth-most abundant mineral in the body and is essential for good health. Magnesium aids the action of the enzymes that facilitate the chemical reactions in the body. Magnesium may also help the airway smooth muscle to relax and help control the body's response to infection. It is found in nuts, cereals, seeds, carrots, spinach and seafood. Omega-3 polyunsaturated fatty acids are essential for good health but are

deficient in most people's diets. Omega-6 fatty acids are also essential but are over-consumed. The ideal ratio of omega-6 to omega-3 in the diet is 4 to 1. However, in the average modern diet the ratio is closer to 20 to 1. Omega-3 fatty acids are found in oily fish and shellfish, soy and leafy vegetables.

A balanced diet

A balanced diet with a high intake of fruit, vegetables and fish reduces the risk of developing lung diseases, especially asthma and COPD. Although the effects of diet on the lungs are still under study, it is clear that the following advice can help to maintain good lung health:

• Eat a balanced diet with a lot of fruit, vegetables and fish

• Reduce salt intake

• Restrict the amount of trans- and omega-6 fatty acids in the diet

• Maintain an ideal weight, with a of BMI 21–30 kg/m2

• Undertake moderate exercise

Nutritional factors are also important in relation to morbidity and mortality in advanced COPD, with reports from diverse clinical settings showing that a low BMI and recent weight loss are major predictors of mortality among patients with COPD. Nutritional intervention aimed at restoring fat-free mass is now recommended and 3 recent meta-analyses of original data have shown benefits from such supplementation. Nutritional intervention in COPD should be integrated into pulmonary rehabilitation, both at an early stage and in end-stage disease when patients are on long-term oxygen therapy and/or non-invasive ventilation.

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