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ESPEN GUIDELINES

ESPEN Guidelines on Enteral Nutrition: Cardiology and Pulmonology ☆

S.D. Anker[a,*], M. John[b], P.U. Pedersen[c], C. Raguso[d], M. Cicoira[e], E. Dardai[f], A. Laviano[g], P. Ponikowski[h], A.M.W.J. Schols[i], DGEM: ☆☆ H.F. Becker, M. Böhm, F.M. Brunkhorst, C. Vogelmeier

[a]*Division of Applied Cachexia Research, Department of Cardiology, Charité-Universitätsmedizin Berlin, CVK, Berlin, Germany*
[b]*Department of Cardiology, Pulmonology und Angiology, Charité-Universitätsmedizin Berlin, CCM, Berlin, Germany*
[c]*The Heart Center, Rigshospitalet, Copenhagen, Denmark*
[d]*Nutrition Clinique, Hopital Cantonal, Geneve, Switzerland*
[e]*Section of Cardiology, Department of Biomedical and Surgical Sciences, University of Verona, Verona, Italy*
[f]*Department of Anaesthesia and Intensive Care, St. Stephen Hospital, Budapest, Hungary*
[g]*Department of Clinical Medicine, University, La Sapienza'' di Roma, Roma, Italy*
[h]*Cardia Department, Military Hospital, Wroclaw, Poland*
[i]*Deparment of Respiratory Medicine, University Hospital Maastricht, Maastricht, The Netherlands*

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Summary These guidelines are intended to give evidence-based recommendations for the use of enteral nutrition (EN) in patients with chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD). They were developed by an interdisciplinary expert group in accordance with officially accepted standards and are based on all relevant publications since 1985. They have been discussed and accepted in a consensus conference.

EN by means of oral nutritional supplements (ONS) or tube feeding (TF) enables nutritional intake to be maintained or increased when normal oral intake is inadequate.

Abbreviations: EN, enteral nutrition. EN is used as a general term to include both ONS and tube feeding. When either of these modalities is being discussed separately this is specified in the text. Normal food/normal nutrition: normal diet as offered by the catering system of a hospital including special diets; PEG, percutaneous endoscopic gastrostomy, RCT, randomized controlled trial

☆For further information on methodology see Schütz et al.[68] For further information on definition of terms see Lochs et al.[69]

*Corresponding author. Tel.: +49 30 450 553462; fax: +49 30 450 553951.
E-mail address: s.anker@cachexia.de (S.D. Anker).

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No data are yet available concerning the effects of EN on cachexia in CHF patients. However, EN is recommended to stop or reverse weight loss on the basis of physiological plausibility. In COPD patients, EN in combination with exercise and anabolic pharmacotherapy has the potential to improve nutritional status and function. Frequent small amounts of ONS are preferred in order to avoid postprandial dyspnoea and satiety as well as to improve compliance.

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Summary of statements: Chronic heart failure (CHF)

Subject	Recommendations	Grade[68]	Number
Indication	EN is recommended in cardiac cachexia to stop or reverse weight loss on the basis of physiological plausibility.	C	1.3
	There is no indication for enteral nutrition (EN) in the prophylaxis of cardiac cachexia.		1.4
Contraindications	There are no specific contraindications. Avoid fluid overload.		1.6

Grade: Grade of recommendation; Number: refers to statement number within the text.

Summary of statements: Chronic obstructive pulmonary disease (COPD)

Subject	Recommendations	Grade[68]	Number
Indication	There is limited evidence that COPD patients profit from EN per se.	B	2.3
	EN in combination with exercise and anabolic pharmacotherapy has the potential to improve nutritional status and function.		2.3
Application	Frequent small amounts of oral nutritional supplements (ONS) are preferred to avoid postprandial dyspnoea and satiety and to improve compliance.	B	2.5
Type of formula	In stable COPD there is no additional advantage of disease specific low carbohydrate, high fat ONS compared to standard high protein or high energy ONS.	B	2.5

Grade: Grade of recommendation; Number: refers to statement number within the text.

1. Chronic heart failure (CHF)

Introduction: Approximately 1% of the population suffers from CHF,[1] from which the average 5-year-survival-rate is approximately 50%.[1] Over the next few years, the general increase in life expectancy, better treatment of acute cardiac events, and improvements in diagnostic and therapeutic management of CHF itself will lead to better survival and therefore an increased prevalence of this disease among the elderly particularly in its advanced form. Since cardiac cachexia will be more common in the future, it is likely that EN will find an increasing place in cardiological practice.

1.1. Does CHF have an influence on nutritional status, and on energy and substrate metabolism?

The prevalence of cardiac cachexia, defined as weight loss of 6% or more in at least 6 months, has been estimated as about 12–15% in patients in New York Heart Association (NYHA) classes II–IV. The incidence of weight loss >6% in CHF

patients with NYHA class III/IV is approximately 10% per year (IIb).

CHF affects nutritional state, energy and substrate metabolism

Comment: CHF is accompanied by complex changes in the neurohormonal and immunological status of the patient, inducing a continuing catabolic state.[2] Comparing CHF patients with and without weight loss, no significant differences have been observed in terms of cardiac function. Among patients in NYHA classes II and III with no overall weight loss, muscle atrophy of the lower limbs is observed in up to 50%.[3]

Cardiac cachexia, which affects 12–15% of CHF patients,[5,8] can be diagnosed if, over 6 months or more, there is weight loss of more than 6.0% (in the absence of oedema) compared to normal premorbid weight.[4] This definition has been validated in the SOLVD and V-HeFT-II study populations.[5] Generalized muscle atrophy of the limbs and significant loss of fat tissue are common in cardiac cachexia,[6] but osteoporosis is rare.[7] The above definition of cardiac cachexia has yet to be tested in the context of surgery in heart failure patients.

Patients with cardiac cachexia have an increased resting energy expenditure,[9] although, due to decreased overall activity, total energy expenditure is reduced by 10–20% compared to CHF patients without cachexia.[10] Neuroendocrine and immunological disturbances underly the altered balance between anabolism and catabolism in these patients[4] with increased plasma levels of catecholamines, cortisol, aldosterone, and rennin,[11] steroid and growth hormone resistance,[12,13] and activation of cytokines.[14,15] Protein malabsorption plays no part in the development of cardiac cachexia,[16] although fat malabsorption could be of importance.[17] It has been estimated that loss of appetite (anorexia) plays a significant role in only 10–20% of all cases of cardiac cachexia.[4] Although detailed studies of food intake and appetite are lacking. Interestingly, a recent study has shown that non-obese, weight stable, free-living patients with clinically stable CHF and a body mass index (BMI) of less than 25 kg/m^2 have a lower intake of calories and protein and expend less energy in physical activity.[18] More research into these issues is necessary.

1.2. Does nutritional status have prognostic significance?

CHF patients with cardiac cachexia have a mortality two to three times higher than non-cachectic CHF patients (IIb).

Comment: Independently of other established markers of CHF prognosis, such as peak oxygen consumption, plasma sodium concentration, left ventricular ejection fraction, and functional NYHA class, the presence of cardiac cachexia predicts a worse prognosis[5,8] (IIb). Since there are no available studies of EN in this condition it is not possible to give a statement on the effect of such therapy on outcome. There are no published epidemiological data available to show that weight gain, by whatever means, improves outcome in this group of patients. However, at the recent American Heart Association meeting in Dallas, USA (November 2005), Anker reported that in the COMET study of 3000 CHF patients in NYHA classes II–IV who were all treated with one of two beta-blockers for a period of 5 years, weight gain was independently associated with significantly better survival and lower hospitalization rates (Anker SD, personal communication).

1.3. Is there an indication for EN in the treatment of cardiac cachexia?

Although there is no evidence available from well designed studies EN is recommended to stop or reverse weight loss on the basis that it improves outcome in other similar conditions and there is a plausible physiological argument for it (C).

Comment: In the absence of good evidence there is an urgent need for controlled studies of nutritional treatment in this condition[4,19–21] (IV) with the aim of improving function through increased supply of nutrients and energy. A further aim of such treatment might also be to complement other therapies, e.g. to supply extra protein during treatment with anabolic steroids, growth factors, or exercise training.

Other forms of nutritional support have been tested in small numbers of patients with cardiac cachexia particularly in those undergoing cardiac surgery, in whom preoperative feeding decreased the number of complications, mortality, and length of postoperative hospital stay[22,23] (III). However, an important disadvantage of these supportive nutritional studies in CHF is the fact that they were all performed in the era before modern standard treatment with angiotensin-converting enzyme inhibitors and beta-blockers. Beta-blockers have proven anti-catabolic effects[24] and in CHF, there is evidence that angiotensin-converting enzyme inhibitors prevent weight loss.[5]

1.4. Is there an indication for EN in the prophylaxis of cardiac cachexia?

Currently there is no indication for EN in the prophylaxis of cardiac cachexia.

Comment: Controlled studies to investigate this question are desirable. These studies should include detailed body composition analyses.

1.5. Is there any known influence of EN on disease progression, survival, and morbidity of CHF patients?

It is not possible to answer this question, because there are no studies available.

Comment: Only one clinical trial has so far evaluated the influence of EN on the physical function of patients with advanced CHF.[25] EN for 24 weeks (compared to no EN), resulted in a greater improvement in exercise capacity (no *P*-value provided), and a significant increase in lean body mass (LBM) ($P = 0.03$) in CHF patients in NYHA class III/IV. However, the scientific reliability of this report could not be assessed completely by the group since the paper was published in Russian. More data are urgently needed in this field.

1.6. Are there any contraindications to EN in patients with CHF?

There are no specific contraindications to EN in CHF patients. Fluid overload must be avoided.

2. Chronic obstructive pulmonary disease (COPD)

2.1. Does COPD have an influence on nutritional state, energy and substrate metabolism?

Between 25% and 40% of patients with advanced COPD are malnourished.

Comment: Clinically relevant weight loss (5% of actual weight within three months or 10% within 6 months) is found in 25–40% of all cases when lung function is severely impaired ($FEV_1 < 50\%$). Muscle wasting, defined as fat-free mass index (FFMI) $< 16\,kg/m^2$ (in males) and $< 15\,kg/m^2$ (in females), is found in 25% of patients with GOLD stages 2 and 3 and in up to 35% of cases with severe disease (GOLD stage 4).[26,27] A French cross-sectional survey in 300 COPD outpatients found LBM depletion in 38% of patients, whereas BMI levels were low ($< 20\,kg/m^2$) in only 17% of patients.[28] LBM was therefore considered the most sensitive tool for detecting undernutrition in COPD patients. A high prevalence of osteoporosis is also observed in these patients.[29]

Partial and global respiratory insufficiency can be caused by a number of different non-malignant lung diseases. COPD, asthma, lung fibrosis, pneumoconiosis, allergic alveolitis, and sarcoidosis leading to progressive impairment of lung function in their advanced stages. The most common cause of chronic respiratory insufficiency is COPD, due to cigarette smoking, affecting more than 1% of the overall population.[30,31] There is limited information regarding nutritional status and metabolic abnormalities in other respiratory diseases apart from COPD.

The causes of cachexia in COPD are multifactorial including tissue hypoxia, ageing, physical exercise, increased resting metabolic rate, chronic inflammatory processes,[32] and certain drugs, resulting in net catabolism.[33,34] Endogenous protective anabolic mechanisms are insufficiently effective, due possibly to hormonal resistance syndromes.[35]

A pronounced loss of appetite (anorexia) and decreased food intake are of central importance in the weight loss which accompanies COPD.[35,36] This is particularly marked during acute exacerbations and may be triggered by difficulties in chewing and swallowing secondary to the altered mechanics of breathing, although hypoxia might also be responsible for appetite loss via the neurohormonal actions of leptin and of cytokines.[37–39]

The resting metabolic rate is increased in a substantial proportion of COPD patients, but is unrelated to total and activity-induced energy expenditure. A specific increase in activity-induced energy expenditure has also been shown to trigger weight loss in COPD.[40]

Linked to absolute or relative loss of fat-free mass, abnormalities in whole body and muscle protein and amino acid metabolism have been described as well as a decreased whole body lipolytic response after beta-adrenergic stimulation.[41] Muscle wasting secondary to reduced nutritional intake increased energy consumption, and treatment with steroids[42,43] also affect the respiratory muscles whose consequent weakness further exacerbates respiratory failure, prevents weaning from ventilators, and impairs outcome of treatment during acute exacerbations.

2.2. Does nutritional status have an influence on prognosis?

Underweight and low fat-free mass are independently associated with a poor prognosis in patients with chronic respiratory insufficiency, especially in COPD (IIb).

Comment: Independently of other factors, weight loss and a low BMI predict a poor survival in COPD

patients.[44–46] Mean survival of COPD patients with both cachexia and an $FEV_1 < 50\%$ is approximately 2–4 years, considerably shorter than those without cachexia (IV).

The prevalence and prognostic importance of weight change in unselected subjects with COPD was examined in the Copenhagen City Heart Study[47] who attended two examinations 5 years apart and were followed for 14 years. After adjusting for age, smoking habits, baseline BMI and lung function, weight loss was associated with higher mortality in persons with and without COPD (rate ratio (RR) for weight loss > 3 BMI units 1.71 (95% confidence interval (CI): 1.32–2.23) and 1.63 (95% CI 1.38–1.92), respectively). In those with severe COPD, there was a significant effect on risk ratio of baseline BMI and weight change: in the normal-to-underweight ($BMI < 25\,kg/m^2$), the best survival was seen in those who gained weight, whereas for the overweight and obese ($BMI \geqslant 25\,kg/m^2$), best survival was seen when weight remained stable. Recent studies indicate that FFMI is an independent predictor of mortality in COPD irrespective of FM.[48–51] This may be related to adverse effects of low FFM on skeletal muscle function,[52] exercise capacity[53] and health status[54] that increase the frequency and severity of acute exacerbations.

2.3. Is there any benefit of EN in the treatment of patients with advanced non-malignant lung diseases?

There is limited evidence that COPD patients profit from EN, although, in combination with exercise and anabolic pharmacotherapy, it has the potential to improve nutritional status and function (B).

Comment: The main aim of treatment is to meet calculated nutritional requirements and prevent weight loss. On the other hand, EN may also have a role as part of an integrated pulmonary (exercise) rehabilitation programme to meet increased energy requirements or to support other therapies (e.g. protein supplementation during treatment with anabolic steroids or growth factors).

While several studies have shown that weight gain can be induced by caloric support in a controlled clinical setting and in some out-patient settings, a recent Cochrane review[55] on caloric supplementation for at least 2 weeks in patients with stable COPD concluded that "*there is no evidence that simple nutritional supplementation helps people in COPD*". Unfortunately this review did not make a distinction between a failure to intervene and a failure of intervention. In some of the papers on which the meta-analysis was based, patients took the prescribed nutritional supplements to replace regular meals rather than adding to them so that the intervention resulted in no increase in energy intake, and no weight gain could therefore be expected. In the studies that did achieve an increase in energy intake, functional improvements were also observed.

Studies to investigate the long-term effect of nutritional support on weight, body composition, functional performance and mortality are needed to judge whether EN, without additional anabolic stimulus, is indicated and what factors[56–58] may limit therapeutic efficacy.

All studies that investigated nutritional support as an integrated part of supervised pulmonary rehabilitation showed positive effects on weight gain.[59–62] Only one of these studies [59] has yet been included in the Cochrane review.

2.4. Is there an influence of EN on disease progression, survival, and mortality in patients with COPD?

Loss of body weight is correlated with increased morbidity and mortality. However, due to the lack of studies on the effects of EN, it is not possible to make a clear recommendation.

Comment: No controlled data are available regarding the effects of long-term nutritional support on disease progression or prognosis in advanced COPD. In one study short-term weight gain (> 2 kg in 8 weeks) was associated with better survival.[46] There is a need to perform long-term studies of balanced EN in cachectic patients with COPD, in a controlled double-blind fashion.

The adverse effect of depletion of FFM per se on mortality, even in weight stable COPD patients indicates that FFM, in particular muscle mass, is an important therapeutic target in these patients. Nutritional support could therefore not only be used to maintain a stable body weight, but could also contribute to inducing muscle anabolism either singly or in combination with exercise and/or pharmacological intervention.

2.5. What type of formula should be used?

In patients with stable COPD there is no additional advantage of disease specific low carbohydrate, high fat ONS over standard or high protein or high energy ONS (B). Frequent smaller amounts of ONS are preferred to avoid postprandial dyspnea and satiety and to improve compliance (B).

Comment: The outcome of EN in COPD may be limited by postprandial dyspnea, satiety and

adverse effects of energy or nutrient load on the ventilatory system. Nutrition and ventilation are intrinsically related because oxygen is required for optimal energy exchange. It was suggested that standard formulae, which are usually rich in carbohydrates (50–60 energy%) would induce greater ventilatory demand due to a higher respiratory quotient. Several randomized controlled studies have compared the acute effects of high (50–100 energy%) and low carbohydrate (30 energy%) content, on immediate postprandial energy metabolism at rest and during exercise in clinically stable COPD patients.[63–66] Adverse effects have indeed been demonstrated with high carbohydrate formulae but only in studies that used amounts of ONS (916 kcal) that exceed the energy content of a normal meal and would therefore be difficult to incorporate into the daily pattern of meal consumption without affecting spontaneous food intake. ONS could also have acute adverse effects on the intake of normal food by delaying gastric emptying time. One study indeed showed adverse effects of a high fat ONS compared to a standard ONS on gastric emptying time[67] and another study showed increased postprandial dyspnea after 250 kcal of a high fat ONS compared to a equicaloric amount of high carbohydrate (= standard) ONS.[63] A more recent study showed positive effects of small portion carbohydrate and protein rich ONS on weight gain after 8 weeks when compared to normal size supplements of similar macronutrient composition[58] (IIb).

Based on the available evidence it is concluded that in clinically stable COPD patients, optimal efficacy of ONS is best achieved not by manipulating macronutrient composition but by giving EN in small frequent doses thereby avoiding complications and improving compliance composition.

For acute respiratory disease syndrome see guidelines Intensive Care chapter.

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