ESPEN Guidelines on Parenteral Nutrition: On Cardiology and Pneumology

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SUMMARY

Nutritional support is becoming a mainstay of the comprehensive therapeutic approach to patients with chronic diseases. Chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) are frequently associated with the progressive development of malnutrition, due to reduced energy intake, increased energy expenditure and impaired anabolism. Malnutrition and eventually cachexia have been shown to have a negative influence on the clinical course of CHF and COPD, and to impinge on patients’ quality of life. Nutritional support in these patients should be therefore considered, particularly to prevent progressive weight loss, since restoration of lean and fat body mass may not be achievable. In CHF and COPD patients, the gastrointestinal tract is normally accessible and functioning. Although recent reports suggest that heart failure is associated with modifications of intestinal morphology, permeability and absorption, the clinical relevance of these are still not clear. Oral supplementation and enteral nutrition should represent the first choices when cardiopulmonary patients need nutritional support, particularly given the potential complications and economic burden of parenteral nutrition. This appropriately preferential enteral approach partly explains the lack of robust clinical trials of the role of parenteral nutrition in CHF and COPD patients. Based on the available evidence collected via PubMed, Medline, and SCOPUS searches, it is recommended that parenteral nutrition is reserved for those patients in whom malabsorption has been documented and in those in whom enteral nutrition has failed.

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Summary of statements: Parenteral Nutrition in Cardiology

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<td>Background</td>
<td>The prevalence of cardiac cachexia, defined from weight loss of at least 6% in 6 months, has been estimated at about 12–15% in patients in New York Heart Association (NYHA) classes II–IV. The incidence of weight loss &gt;6% in CHF patients with NYHA class III/IV is approximately 10% per year. CHF affects nutritional state, energy and substrate metabolism. The mortality in CHF patients with cardiac cachexia is 2–3 times higher than in non-cachetic CHF patients. Although there is limited evidence that gut function is impaired in CHF, decreased cardiac function can reduce bowel perfusion and lead to bowel wall oedema, resulting in malabsorption.</td>
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<td>Indications</td>
<td>Although there is no evidence available from well-designed studies, PN is recommended to stop or reverse weight loss in patients with evidence of malabsorption, on the basis that it improves outcome in other similar conditions and there is a plausible physiological argument for it. Currently there is no indication for PN in the prophylaxis of cardiac cachexia. Further studies are needed to assess the impact of the parenteral administration of specific substrates on cardiac function.</td>
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**1. Chronic heart failure**

**1.1. Introduction**

The prevalence of CHF among the general population is approximately 1% and 2%, and the average 5-year survival-rate is approximately 50%.

Considering the improvement in diagnostic tools and the advances in treatment opportunities which will likely occur during the next few years, it is expected that the survival of patients suffering from chronic heart failure (CHF) will increase.

Therefore, the prevalence of this disease among the elderly, particularly in its advanced form, is likely to increase. Since malnutrition and eventually cardiac cachexia (i.e., weight loss associated with increased inflammatory response, and impaired metabolic response to starvation) will be more common in the future, and nutritional support will necessarily find an increasing place in cardiological practice.

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

The etiology of heart failure is complex and involves factors such as neurohormonal changes, metabolic abnormalities, and increased substrate utilization. The cardiac pump function is impaired, leading to decreased cardiac output and reduced tissue perfusion.

Patients with cardiac cachexia have increased resting energy expenditure, although due to decreased overall activity, total energy expenditure is reduced by 10–20% compared to CHF patients without cachexia. Neuroendocrine and immunological disturbances underlie the altered balance between anabolism and catabolism in these patients, with increased plasma levels of catecholamines, cortisol, aldosterone, and renin.

Protein malabsorption plays no part in the development of cardiac cachexia, although fat malabsorption could be of importance. It has been estimated that loss of appetite (anorexia) plays a significant role in only 10–20% of all cases of cardiac cachexia, although detailed studies of food intake and appetite are lacking. Recently, a 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/m² have a lower intake of calories and protein and expend less energy in physical activity.

**1.3. Does nutritional status have prognostic significance?**

The mortality in CHF patients with cardiac cachexia is 2–3 times higher than in non-cachectic CHF patients.

Comments: 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, 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/m² have a lower intake of calories and protein and expend less energy in physical activity.

**1.4. Is gut function impaired by CHF?**

Although there is limited evidence that gut function is impaired in CHF, decreased cardiac function can reduce bowel perfusion and lead to bowel wall oedema, resulting in malabsorption.

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**Summary of statements: Parenteral Nutrition in Cardiology**

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<tr>
<td>Contra-indications</td>
<td>There are no specific contraindications to PN in CHF patients. However, considering that cardiac function is decreased and water retention is frequently found in CHF patients, it is recommended that PN should be avoided, other than in patients with evidence of malabsorption in whom enteral nutrition has been shown, or is strongly expected, to be ineffective.</td>
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<td>Implementation</td>
<td>When feeding CHF patients, either enteral or parenterally, fluid overload must be avoided.</td>
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**Summary of statements: Parenteral Nutrition in Respiratory Medicine**

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<td>Background</td>
<td>Between 25% and 40% of patients with advanced COPD are malnourished. Being underweight and having low fat-free mass are independently associated with a poor prognosis in patients with chronic respiratory insufficiency, especially in COPD.</td>
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<td>Indications</td>
<td>There is no evidence showing that gut function is impaired in COPD patients. Therefore, considering that enteral nutrition is less expensive and associated with fewer and less severe complications than parenteral nutrition, enteral nutrition should represent the first approach to patients with COPD in need of nutritional support. There is limited evidence that COPD patients intolerant of EN profit from PN. Small studies do however suggest that, in combination with exercise and anabolic pharmacotherapy, PN has the potential to improve nutritional status and function.</td>
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<td>Effect of PN</td>
<td>Loss of body weight is correlated with increased morbidity and mortality. However, due to the lack of studies of its effects, it is not possible to be sure if prognosis is influenced by the provision of PN. In patients with stable COPD, glucose-based PN causes an increase in the respiratory CO₂ load. PN composition should accordingly be orientated towards lipids as the energy source. There is not sufficient evidence to recommend specific lipid substrates.</td>
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<td>Regimen</td>
<td>In patients suffering from chronic heart failure (CHF) will increase. If heart failure management and functional NYHA class II–IV are approximately 10% per year (B). CHF affects nutritional state, energy and substrate metabolism (B).</td>
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1.5. Is PN indicated in the treatment of cardiac cachexia?

Comments: in recent research, the gut has received very little attention from cardiologists as its role in the pathogenesis of cardiovascular disease is usually minor. However, it is acknowledged that decreased cardiac function may reduce bowel perfusion and therefore impair the function of gut barrier. Evidence exist suggesting that a “leaky” bowel wall may lead to translocation of bacteria and/or endotoxins, which in turn may sustain the inflammatory cytokine activation in CHF and exacerbate its detrimental effects on nutritional status. Decreased cardiac function may lead to bowel wall oedema and thus malabsorption, which may prevent, at least in patients with advanced CHF, digestion and absorption of food and/or enteral diets. Recent data obtained from 22 patients with cardiac failure show that CHF is a multisystem disorder in which intestinal morphology, permeability and absorption are modified (III).

1.6. Is there an indication for PN in the prophylaxis of cardiac cachexia?

Currently there is no indication for PN in the prophylaxis of cardiac cachexia (Grade C). Further studies are needed to assess the impact of the parenteral administration of specific substrates on cardiac function.

Comments: PN in general does not seem to offer useful prophylaxis. There are however data on L-arginine (Arg), the substrate for the synthesis of nitric oxide (NO), which stimulates angiogenesis, and inhibits leukocyte adhesion, platelet aggregation, and superoxide generation. Arg also has NO-independent effects, including synthesis of creatine, proline and polyamines, and secretion of insulin and growth hormone. Preliminary evidence from seven patients with severe congestive cardiac failure indicates that intravenous Arg (30 g in 30 min) may reduce heart rate and improve haemodynamics. Parenteral administration of Arg also appears able to reverse some of the endothelial dysfunction associated with major cardiovascular risk factors (III). However, intravenous Arg is not currently available for clinical use and confirmatory data are clearly needed in this field.

1.7. Is there any known influence of PN on the disease progression, survival, and morbidity of CHF patients?

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

1.8. Are there any contraindications to PN in patients with CHF?

There are no specific contraindications to PN in CHF patients. However, considering that cardiac function is decreased and water retention is frequently found in CHF patients, it is recommended that PN should be avoided, other than in patients with evidence of malabsorption in whom enteral nutrition has been shown, or is strongly expected, to be ineffective (B). When feeding CHF patients, either enterally or parenterally, fluid overload must be avoided (C).

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 (B).

Comments: clinically relevant weight loss (5% within three months, or 10% within 6 months) is found in 25–40% of all cases in whom lung function is severely impaired (FEV1 < 50%). Muscle wasting, defined as fat-free mass index (FFMI) < 16 kg/m² in males, and < 15 kg/m² 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) (IIb). A French cross-sectional survey of 300 COPD outpatients on long-term oxygen therapy found FFM depletion in 38% of patients, whereas BMI levels were low (<20 kg/m²) in only 17% of patients (IIb). FFM is therefore considered the most sensitive tool for detecting wasting in COPD patients. A high prevalence of osteoporosis is also observed in these patients (IIb).

COPD, usually due to cigarette smoking, is the most common cause of chronic respiratory insufficiency, affecting more than 1% of the world’s population. Respiratory insufficiency can also be caused by a number of other non-malignant lung diseases, including asthma, lung fibrosis, pneumoconiosis, allergic alveolitis, and sarcoidosis, which lead to progressive impairment of lung function in their advanced stages. There is limited information regarding nutritional status and metabolic abnormalities in these conditions. The causes of cachexia in COPD are thought to be multifactorial, and include tissue hypoxia, ageing, physical inactivity, increased resting metabolic rate, chronic inflammatory processes, and certain drugs, resulting in net catabolism and muscle wasting. Endogenous protective anabolic mechanisms are insufficiently effective, due possibly to hormonal resistance syndromes. A pronounced loss of appetite (anorexia) and decreased food intake are of central importance in the weight and fat loss which accompany COPD (IIb). 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 neurohumoral actions of leptin and cytokines. 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 (IIb). 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. Muscle wasting...
secondary to reduced nutritional intake increases energy consumption, and treatment with steroids also affects 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?

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

Comments: independently of other factors, weight loss and a low BMI predict poor survival in COPD patients (IIb). Mean survival of COPD patients with both cachexia and an FEV1 < 50% is 2–4 years, considerably shorter than in those without cachexia.

The prevalence and prognostic importance of weight change in unselected subjects with COPD was examined in the Copenhagen City Heart Study. Individuals attended two examinations 5 years apart and were then followed for 14 years. After adjusting for age, smoking habits, baseline BMI and lung function, weight loss was associated with higher mortality in those with and without COPD (IIb). In those with severe COPD, the baseline BMI and subsequent weight change had significant effects on risk ratios. In the normal-to-underweight (BMI < 25 kg/m²), the best survival was seen in those who gained weight, whereas for the overweight and obese (BMI > 25 kg/m²), best survival was seen when weight remained stable. Recent studies indicate that FFMI is an independent predictor of mortality in COPD irrespective of FM (IIb). This may be related to adverse effects of low FFM on skeletal muscle function, exercise capacity, and overall health status, that increase the frequency and severity of acute exacerbations.

2.3. Is gut function impaired by COPD?

There is no evidence showing that gut function is impaired in COPD patients. Therefore, considering that enteral nutrition is less expensive and associated with fewer and less severe complications than parenteral nutrition, enteral nutrition should represent the first approach to patients with COPD in need of nutritional support (B).

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

There is limited evidence that COPD patients intolerant of EN profit from PN. Small studies do however suggest that, in combination with exercise and anabolic pharmacotherapy, PN has the potential to improve nutritional status and function (C).

Comments: Dyspnoea is one of the main symptoms of COPD patients. Dyspnoea may significantly reduce food intake. Consequently, COPD patients may not meet their nutritional requirements with food or oral supplements. Also, enteral feeding tubes may reduce ventilation and worsen dyspnoea. Therefore, in COPD patients who are intolerant to enteral feeding, PN may provide an opportunity to provide the correct amounts of macro- and micronutrients. Only a few studies have investigated the role of PN in replenishing COPD patients. Sucher et al. demonstrated that the administration of PN combined with growth hormone improved nitrogen balance in severely malnourished COPD patients (IIb). Aguilaniu et al. demonstrated that hypercaloric (55 kcal/kg/d), high-lipid (55%) parenteral nutrition improved nitrogen balance in COPD patients (IIb). However, the small number of patients enrolled (six and eight, respectively) limits the confidence to be drawn from the results. More studies are needed in this field.

Artificial nutrition may 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). A recent Cochrane review on caloric supplementation for at least 2 weeks in patients with stable COPD concluded that “nutritional support has no effect on anthropometric measures, lung function or exercise capacity in patients with stable COPD” (Ia). Unfortunately this review did not make a distinction between a failure to intervene and a failure of intervention. In the studies that did achieve an increase in energy intake, functional improvements were also observed. Therefore, additional studies are needed to investigate whether PN, by providing nutritional support while minimally influencing food intake, may lead to improved nutritional status of COPD patients.

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

Loss of body weight is correlated with increased morbidity and mortality (Grade B). However, due to the lack of studies of its effects, it is not possible to be sure if prognosis is influenced by the provision of PN.

Comments: no controlled data are available regarding the effects of long-term nutritional support on disease progression or prognosis in advanced COPD. Although in one study short-term weight gain (>2 kg in 8 weeks) was associated with better survival, the SUPPORT study revealed that parenteral hyperalimentation was associated with decreased survival only in acute respiratory failure (IIb). There is a need to perform long-term studies of PN in cachectic patients with COPD, in a controlled double-blind fashion. The adverse effect of depletion of FFM 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 be used not only to maintain stable body weight, but also to contribute to induction of muscle anabolism either on its own or in combination with exercise and/or pharmacological interventions.

2.6. What type of formula should be used?

In patients with stable COPD, glucose-based PN causes an increase in the respiratory CO₂ load. PN composition should accordingly be orientated towards lipids as the energy source (B). There is not sufficient evidence to recommend specific lipid substrates.

Comments: glucose-based PN increases arterial CO₂ concentrations, especially if the glucose load is in excess of metabolic capacity, and it can thus be harmful to patients with COPD. By preferentially selecting lipids as the energy source, the respiratory quotient can be lowered. The proportion of lipid-derived non-protein calories should probably be at least 35% (but probably not more than 65%).

Only one study has investigated the effects on clinical parameters of the provision of specific lipid substrates. Iovinelli et al. recently reported that ventilated patients with COPD receiving PN containing a mixture of soybean derived long-chain triglycerides (LCT) and medium-chain triglycerides (MCT) had a shorter weaning time from mechanical ventilation than patients receiving pure LCT-based PN (Ia). Due to the limited number of patients enrolled in this study, confirmatory data are needed before specific recommendations could be made.
Conflict of interest

Conflict of interest on file at ESPEN (espenjournals@espen.org).

References