Nutrition and Sport

Module 37.4

Physical Activity in Chronic Diseases

Laurence Genton, MD, Internal Medicine, Clinical Nutrition University Hospital, Rue Micheli-du-Crest 24, 1211 Geneva, Switzerland

Learning Objectives

- Impact of physical exercise and physical fitness on the primary prevention of chronic diseases;
- Characteristics of physical exercise advised for the primary prevention of chronic diseases;
- Impact of physical exercise and physical fitness on the secondary prevention of selected chronic diseases;
- Impact of physical exercise and nutritional support of selected chronic diseases.

Contents

1. Introduction
2. Physical activity for the primary prevention of chronic diseases
   2.1. Benefits of physical activity
   2.2. Adverse effects of physical activity
   2.3. Recommendations of physical activity
      2.3.1. Recommendations for adults aged 19-64 yrs
      2.3.2. Recommendations for adults aged ≥ 65 years
   2.4. Physical activity and energy intakes for health-related physical fitness
   2.5. Summary
3. Physical activity for secondary prevention of CD associated with cachexia
   3.1. Chronic heart failure (CHF)
      3.1.1. CHF and physical fitness
      3.1.2. Impact of physical activity on CHF
      3.1.3. Impact of physical activity and nutrition on CHF
      3.1.4. Contraindication of physical activity in CHF
      3.1.5. Recommendations of physical activity in CHF
   3.2. Chronic obstructive pulmonary disease (COPD)
      3.2.1. COPD and physical fitness
      3.2.2. Impact of physical activity on COPD
      3.2.3. Impact of physical activity and nutrition on COPD
      3.2.4. Contraindications of physical activity in COPD
      3.2.5. Recommendations of physical activity in COPD
   3.3. Physical activity for secondary prevention of cancer
      3.3.1. Cancer and physical fitness
      3.3.2. Impact of physical activity on cancer
      3.3.3. Impact of physical activity and nutrition on cancer
      3.3.4. Contraindications of physical activity in cancer
      3.3.5. Recommendations of physical activity in cancer
   3.4. Summary
4. References
Key messages

- Physical fitness includes body composition, muscle strength and endurance, cardiorespiratory fitness and flexibility;
- Regular physical activity has numerous effects on physical fitness and cardiometabolic risk and can prevent the development of some chronic diseases;
- The benefits of regular physical activity outweigh the potential harm in healthy subjects;
- Guidelines recommend regular aerobic and resistance training for healthy adults, and additionally neuromotor training in older persons;
- The addition of regular physical activity to a hypo- or hypercaloric diet modulates physical fitness;
- Regular physical activity positively affects physical fitness and clinical outcome in patients with heart failure, chronic obstructive pulmonary disease and cancer;
- Multimodal treatment combining physical activity and nutritional support improves outcome in COPD patients;
- No studies evaluated the impact of physical activity and nutritional support in cachectic heart failure or cancer patients but several studies on this topic are presently on-going;
- Some recommendations for physical activity are available for heart failure and cancer patients.
1. Introduction

Physical activity is defined as any body movement produced by skeletal muscle that increases energy expenditure. It includes activities performed at work, for transport, domestic duties and leisure time.

Noncommunicable chronic diseases, termed for ease as chronic diseases (CD), are the cause of over 60% of deaths overall (1). The mortality related to CD is expected to rise in the next decades and cause over 75% of deaths by 2030 (2). The major CD related with mortality are cardiovascular diseases, respiratory diseases, cancer, mental illness and diabetes (3). Furthermore, CD lead to an increased economical burden related to healthcare consumption and loss of labour days, estimated as US $ 47 trillions for the period of 2011-2030 worldwide (4).

The World Health Report, undertaken by the World Health Organization (WHO), reported the 10 main risk factors related to CD burden (5). In developed countries, the four major modifiable risk factors are poor diet, physical inactivity, smoking, and harmful alcohol use.

This module focuses on the importance of physical activity in the primary prevention of NCD, and in the secondary prevention of selected CD associated with cachexia in combination with nutritional support, when available.

2. Physical Activity for Primary Prevention of CD

Functional capacities associated with health and disease prevention define health-related physical fitness. They are often used as outcome when evaluating the impact of physical activity. Interestingly, cardiorespiratory fitness may better represent habitual physical activity than self-reported physical activity (6). Components of health-related fitness are reported on Table 1.

<table>
<thead>
<tr>
<th>Table 1 Components of health-related physical fitness</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>Body composition</td>
<td>Structural components of the body</td>
</tr>
<tr>
<td>Muscular strength</td>
<td>Maximum force generated by a muscle</td>
</tr>
<tr>
<td>Muscular endurance</td>
<td>Ability of a muscle to perform repeated contractions for a prolonged period of time</td>
</tr>
<tr>
<td>Cardio-respiratory fitness</td>
<td>Ability of the circulatory and respiratory systems to supply oxygen to skeletal muscle for energy-generating processes</td>
</tr>
<tr>
<td>Flexibility</td>
<td>Ability to move joints and muscle freely through their full range of motion</td>
</tr>
</tbody>
</table>

*1RM: one repetition maximum or maximum weight a person can lift in a single repetition.
VO2 max: highest oxygen consumption attainable by an individual.

Recently, the American College of Sports Medicine (ACSM) recognized also the importance of neuromotor fitness for public health (7). It includes agility, balance, coordination, reaction time, power and speed.
2. 1. Benefits of Physical Activity

Planned, structured and repetitive physical activity performed to maintain or improve health and fitness is termed physical exercise. Physical exercise is classified as aerobic (endurance), resistance, flexibility and neuromotor training and is characterized by frequency, intensity, time and type (mnemonically FITT).

The benefits depend on the characteristics of the performed physical exercise. They have been studied mostly with regard to body composition, muscular fitness and cardiorespiratory fitness and are summarized in Fig. 1. The ACSM reports a grade A evidence level for the impact of aerobic and resistance training on overall physical fitness and health, and for the impact of flexibility training on maintenance and improvement of joint range motion, and a grade B evidence level for the impact of neuromotor training on risk and fear of falling in older people (7).

![Physical activity]

**Fig. 1** Impact on health-related physical fitness and cardiometabolic risk factors (7, 8)

Chodzko et al. summarized the benefits of aerobic and resistance training on the prevention of specific NCD (9).

### Table 2

**Benefits on prevention of CD (9)**

<table>
<thead>
<tr>
<th>Type of exercise</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aerobic and resistance training</td>
<td>Coronary heart disease</td>
</tr>
<tr>
<td></td>
<td>Possibly chronic renal failure and congestive heart failure</td>
</tr>
<tr>
<td>Aerobic training</td>
<td>Cancer, cognitive impairment, depression</td>
</tr>
<tr>
<td></td>
<td>disability, hypertension, obesity, osteoporosis, peripheral vascular diseases, stroke, type 2 diabetes</td>
</tr>
<tr>
<td>Resistance training</td>
<td>Impaired glucose tolerance</td>
</tr>
</tbody>
</table>

↓ weight, total body fat, visceral fat
↑ bone mineral density
↑ or → muscle strength
↑ VO₂ max
↓ or → systolic and diastolic blood pressure
↓ glucose intolerance, insulin resistance
↓ dyslipidemia
↓ or → plasma LDL cholesterol
↑ or → plasma HDL cholesterol
↓ triglycerides

↓ total body fat
↑ lean body mass, bone mineral density
↑ muscle strength
↓ risk of functional limitation
↑ or → VO₂ max
↓ glucose intolerance, insulin resistance
↑ or → plasma LDL cholesterol
↑ or → plasma HDL cholesterol
↑ or → triglycerides

↓ total body fat
↑ lean body mass, bone mineral density
↑ muscle strength
↓ risk of functional limitation
↑ or → VO₂ max
↓ glucose intolerance, insulin resistance
↑ or → plasma LDL cholesterol
↑ or → plasma HDL cholesterol
↑ or → triglycerides

↑ postural stability
↑ balance

↑ balance
↑ agility
↑ muscle strength
↑ risk and fear of falling

↑ balance
↑ agility
↑ muscle strength
↑ risk and fear of falling

↑ balance
↑ agility
↑ muscle strength
↑ risk and fear of falling
2. 2. Adverse Effects of Physical Activity

Adverse effects may occur with physical activity but the potential benefits of physical activity outweigh the harms.

The most common adverse effects are musculo-skeletal injuries but they are generally not severe. Rhabdomyolysis may occur with strenuous exercise. It generally resolves spontaneously but in rare cases, especially in hot conditions, leads to acute renal failure (10).

Sudden cardiac death is rare but can result from congenital cardiovascular abnormalities in young people and from coronary artery disease in older people (11). In healthy adults, the relative risk of acute myocardial infarction and cardiac arrest increases during vigorous exercise, especially in the least active people. The American College of Cardiology and the American Heart Association (AHA) recommend exercise testing before beginning vigorous exercising in asymptomatic men >45 years and women >55 years, asymptomatic persons with diabetes mellitus, or persons with known cardiovascular disease (11).

2. 3. Recommendations of Physical Activity

2. 3. 1. Recommendations for Adults Aged 19-64 years

The following table summarizes the recommendations of the WHO, for adults aged 19 to 65 years (12). Moderate and vigorous intensity correspond to intensities of 5 to 6 and 7 to 8, respectively, on a scale of 0 to 10, or to intensities of 3.0 to 5.9 and ≥ 6 metabolic equivalents.

<table>
<thead>
<tr>
<th>Aerobic exercise</th>
<th>Resistance exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>Several days/wk</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>Moderate and/or vigorous intensity</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>150 min/wk: moderate intensity or 75 min/wk: vigorous intensity or an equivalent combination of both</td>
</tr>
<tr>
<td><strong>Type</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>Pattern</strong></td>
<td>Bouts of ≥ 10 min</td>
</tr>
</tbody>
</table>

The WHO recognizes that the amount of physical activity necessary for CD prevention may vary according to the considered CD but reports that presently there is not enough evidence to establish separate guidelines for each CD. Several national societies also published their recommendations (7, 8), sometimes with regard to specific diseases. They are often more precise regarding the pattern of resistance exercise and may contain recommendations regarding flexibility and balance exercise.

2. 3. 2. Recommendations for Adults Aged ≥ 65 years

The WHO additionally recommends neuromotor training ≥ 3 days/wk to prevent falls and, for the elderly who cannot sustain the recommended volume of exercise, recommends
being as physically active as possible (12). The ACSM and the AHA provide similar recommendations (Table 4) (9, 13).

### Table 4

<table>
<thead>
<tr>
<th>Recommendations for older people (&gt;65y) (ACSM, AHA) (9, 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aerobic exercise</strong></td>
</tr>
<tr>
<td>Frequency</td>
</tr>
<tr>
<td>Intensity</td>
</tr>
<tr>
<td>Duration</td>
</tr>
<tr>
<td>Type</td>
</tr>
</tbody>
</table>

### 2.4. Physical Activity and Energy Intakes for Health-related Physical Fitness

The afore-mentioned recommendations of physical activity do not take into account concomitant calorie intakes. This chapter focuses only on the combined effect of physical activity and nutrition on health-related physical fitness in health subjects.

A review summarized the studies which have investigated the effect of dietary restriction plus exercise on weight loss and body composition (14). It highlights that the combination of modest calorie restriction and physical exercise is preferable over dietary restriction alone to induce weight and fat mass loss and possible preservation of fat-free mass. An older meta-analysis included studies with at least one group submitted to a physical exercise intervention and one group who was not. It showed that for a weight loss of 10 kg, the expected loss of fat-free mass was only 1.7 kg with an intervention combining diet plus exercise as opposed to approximately 2.5 kg with diet alone (15). Physical activity associated with dietary restriction also improves other parameters of health-related physical fitness as muscle strength and aerobic capacity in normal- or overweight subjects (16).

When combined with physical exercise, especially resistance training, hypercaloric intakes may increase the proportion of weight gained as fat-free mass. Rozenek et al included 73 healthy non obese men which were put on a high calorie supplement (2010 kcal/j) or no supplement for 8 weeks in addition to their normal diet, and a 4d/wk resistance training. The supplemented group showed a weight gain of 3 kg consisting almost exclusively of fat-free mass (17) while weight did not change in the control group. Even older subjects can increase their muscle mass and function in case of energy supplementation and simultaneous resistance training (18).
2. 5. Summary

Physical activity to prevent NCD should combine endurance and resistance training several days per week. In older people, neuromotor training is additionally advised. The addition of physical activity to hypocaloric diet enhances the maintenance of fat free mass and may improve muscular and aerobic performance in overweight subjects. The addition of physical activity to hypercaloric diets increase the proportion of weight gain as fat-free mass and likely increases muscle function.

3. Physical Activity for Secondary Prevention of CD Associated with Cachexia

This chapter aims at highlighting the importance of physical activity, in addition to nutritional support, in the management of some chronic diseases associated with cachexia. Cachexia is defined by “a complex syndrome associated with underlying illness and characterized by loss of muscle with or without loss of fat mass” (19). We will focus on chronic heart failure, chronic obstructive pulmonary disease (COPD) and cancer as they are among the major NCD related with mortality.

3. 1. Chronic Heart Failure (CHF)

Cachexia occurs in 16% of patients with CHF when defined by a weight loss of > 7.5% (20) or 36% when defined by a weight loss of > 6% (21). When using nutritional indexes, the prevalence of malnutrition lies between 60 and 69% (22).

3. 1. 1. CHF and Physical Fitness

Patients with CHF experience early fatigue, exertional dyspnea and decreased exercise tolerance, indicating a decreased cardiorespiratory fitness. They have a decreased number of type I fibers, mitochondrial volume, capillary density and oxidative enzymes, and an increased number of type II fibers and glycolytic enzymes in the limbs (23). These alterations likely contribute to decreased muscle mass, muscle strength and endurance (24), and to a shift from aerobic to anaerobic metabolism. In cachectic CHF patients, muscle strength and mass are lower, fatigability is higher and peak oxygen consumption is similar compared to non cachectic CHF patients (25). The relationship between CHF and physical fitness is bidirectional since a decreased cardiorespiratory fitness has been associated with a higher risk of CHF (26) and CHF-associated mortality (27) in subjects healthy at baseline, and of mortality in subjects with CHF (28). Interestingly, cardiorespiratory fitness may better predict cardiovascular events than physical activity (29).

3. 1. 2. Impact of Physical Activity on CHF

Aerobic training with or without resistance training has the following effects (23, 30):
- Heart: no major effect on cardiac function.
- Lung: ↓ rate of ventilation and CO2 production.
- Skeletal muscle: ↑ endurance exercise capacity, oxidative metabolism and muscle strength.
- Vessels: ↑ angiogenesis and muscle capillary density.
- Neurohormonal, immune and autonomic function: ↓ resting levels of angiotensin, aldosterone, vasopressin, atrial natriuretic peptide; ↓ RR interval variability; ↓ systemic and muscular pro-inflammatory cytokine expression.
- Quality of life: ↑ quality of life, ↓ anxiety and depression.
A recent meta-analysis included randomized controlled trials comparing exercise vs. usual care with a minimum follow-up of 6 months, in patients with systolic heart failure (31). Exercise led to a reduced risk of hospitalization and improved quality of life. There was no impact on all-cause mortality at 12 months but a trend towards reduced mortality in the longer term.

It has been suggested that moderate exercise is safe in cachectic CHF (32). Exercise capacity, evaluated through peak oxygen consumption, is positively correlated with peak leg blood flow in cachectic CHF patients and with muscle strength and age in non cachectic CHF patients (25).

3. 1. 3. Impact of Physical Activity and Nutrition on CHF

There is presently no good evidence for the use of enteral nutrition to treat cardiac cachexia. However, the ESPEN guidelines recommend using enteral nutrition in patients with cardiac cachexia as it improves outcome in patients with cachexia of other etiologies (33).

Studies on the combined impact of nutritional support and physical activity in cachectic patients with CHF are not available. However, a multicenter trial (Nutricard; ClinicalTrial.gov NCT#01864733) is presently evaluating the impact of a multimodal strategy including physical exercise (aerobic and resistance), oral nutritional supplements, omega-3-fatty acids and testosterone on physical fitness, in cachectic CHF patients.

3. 1. 4. Contraindication of Physical Activity in CHF

According to a consensus document of the AHA and the European Association for Cardiovascular Prevention and Rehabilitation, exercise testing and training is contraindicated in the following situations (34):
- Illnesses in the acute phase: coronary syndrome (up to 2 days), heart failure, myocarditis and pericarditis, systemic illness, thrombophlebitis, recent embolism.
- Untreated life-threatening arrhythmias, advanced atrioventricular block.
- Symptomatic aortic stenosis.
- Severe hypertrophic obstructive cardiomyopathy.
- Worsening of exercise tolerance or dyspnea at rest in the last 3 to 5 days.
- Ischaemia during low-intensity exercise.
- Uncontrolled diabetes or hypertension.

3. 1. 5. Recommendations of Physical Activity in CHF

Guidelines recommend aerobic training for stable patients with heart failure of New York Heart Association (NYHA) class I-III, associated or not with resistance training.
Table 5  
Recommendations for patients with CHF (34, 35)

<table>
<thead>
<tr>
<th></th>
<th>Aerobic exercise</th>
<th>Resistance exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>3 to 5 days/wk</td>
<td>2 d/wk</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>Moderate to high intensity</td>
<td>30-40% 1-RM at start, increasing to 40-60% 1-RM</td>
</tr>
<tr>
<td></td>
<td>40-50% of VO$_2$peak at start, increasing to 70-80% VO$_2$peak or HRR of 40-70%</td>
<td>&lt; 15 on Borg RPE scale</td>
</tr>
<tr>
<td></td>
<td>10-14 on Borg RPE scale</td>
<td></td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>20 to 60 minutes/session</td>
<td>-</td>
</tr>
<tr>
<td><strong>Type</strong></td>
<td>Continuous (or interval training)</td>
<td>1-2 sets, 12-25 repetitions</td>
</tr>
<tr>
<td><strong>Pattern</strong></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Remark</strong></td>
<td>Deconditioned patients:</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2x/week, low intensity, 5-10 min/session</td>
<td>Increase in duration before increase in number of sessions.</td>
</tr>
</tbody>
</table>

VO$_2$ peak: highest VO$_2$ consumption on a particular exercise test  
HRR: heart rate reserve = difference between maximal heart rate and peak heart rate  
Borg Rating of Perceived Exertion Scale (Borg RPE): score of 6 to 20, where 20 is maximal effort

While the benefits of physical activity in CHF are well established, adherence to physical activity programs remains problematic.

3.2. Chronic Obstructive Pulmonary Disease (COPD)

The prevalence of malnutrition ranges from 20% in stable COPD outpatients to 35% in candidates for pulmonary rehabilitation (36).

3.2.1. COPD and Physical Fitness

Patients with COPD also suffer from exertional dyspnea and decreased exercise tolerance, compatible with a decreased cardiorespiratory fitness, as CHF patients. They present with muscle atrophy and weakness, shift from type I to type II muscle fibers, a decreased muscular capillary density, decreased mitochondrial density and function, and low oxidative capacity in the limbs (37). A low cardiorespiratory fitness and limb muscle dysfunction in COPD patients, is associated with a higher risk of all-cause mortality (37, 38).

3.2.2. Impact of Physical Activity on COPD

Physical activity decreases the risk of COPD exacerbation and mortality (39). Although the direction of the relationship is unclear, physical activity has also been associated with consistent improvements in the following outcomes:
- dyspnea
- exercise capacity
- gas exchanges
- hyperinflation
- systemic inflammation
- quality of life
The increase in exercise capacity in response to physical activity is similar between cachectic and non cachectic COPD patients, although the quantitative and qualitative remodelling in muscle fibers may differ (40).

3.2.3. Impact of Physical Activity and Nutrition on COPD

There seem to be limited benefit of enteral nutrition alone on outcome in COPD patients (33). However, nutritional support combined with physical activity and possibly other ergogenic interventions (testosterone, omega-3 fatty acids, essential amino acids...) improves outcome in cachectic patients.

Two studies showed that oral nutritional supplements combined with physical exercise held more benefits than usual care in malnourished COPD patients. In the first study, this treatment increased inspiratory pressure, quadriceps strength, 6-min walking distance and health status and decreased IL-6, IL-8 and TNF-alpha decreased after 12 weeks (41). The other study, performed over 4 months confirmed the improvement in exercise capacity and muscle strength, and additionally showed lower hospitalisation costs with this intervention (42).

The combination of pulmonary rehabilitation and nutritional support seems better than physical exercise alone. Indeed, malnourished COPD patients increase their fat-free mass and mid-thigh cross-sectional area more when submitted to the combined treatment (43).

Finally, two studies suggest that outcome may further be improved by the addition of anabolic steroids to oral nutritional support and physical exercise. Schols et al. randomized 233 malnourished COPD to oral nutritional supplements with or without anabolic steroids (AS) for 8 weeks (44). All patients underwent a standardized exercise program. Both treatments resulted in the same weight gain, but the AS group gained more fat-free mass and maximal inspiratory pressure. Pison et al. randomized 122 malnourished patients with chronic respiratory failure, for 3 months, to a multimodal treatment (testosterone, oral nutritional supplements and physical exercise) or solely home education. Patients who underwent the multimodal treatment increased weight, fat-free mass, exercise tolerance, 15-month survival, and, in women, quality of life (45).

3.2.4. Contraindications of Physical Activity in COPD

According to an official American Thoracic Society/European Respiratory Society Statement, contraindications to pulmonary rehabilitation is “any condition that would place the patient at substantially increased risk during pulmonary rehabilitation or any condition that would substantially interfere with the rehabilitative process” (46). It includes of course the conditions mentioned in chapter 3.1.4.

3.2.5. Recommendations of Physical Activity in COPD

Physical exercise is recommended for any patient with chronic respiratory failure (46). The mainstay of exercise training is aerobic exercise which should be performed 3 to 5 days/week, 20-60 minutes/session continuously as in healthy adults, with an intensity of 4 to 6, according to the Borg dyspnea or fatigue score (out of 10) or of 12 to 14 according to the Borg Rating of Perceived Exertion Scale (out of 20)(46). Walking and biking are optimal types of training. Interval training corresponds to high intensity training alternating with periods of rest or lower intensity. It seems to achieve similar results to continuous training when considering exercise capacity, quality of life and skeletal muscle adaptation. It may be an option, especially in patients unable to tolerate the duration or intensity recommended for continuous exercise.

The addition of resistance to aerobic training improves exercise capacity and muscle strength to a greater extent than either training modality alone. Due to the lack of COPD-
oriented guidelines, clinicians generally follow the scheme recommended for healthy adults, i.e. 2 to 4 sets of 8-12 repetitions, on 2-3 days/week (Table 3). Flexibility exercises, at least 2-3 days/week may be useful to improve postural abnormalities.

3. 3. Physical Activity for Secondary Prevention of Cancer

Weight loss occurs mostly in solid tumours, especially of the digestive tract (47). For instance, the incidence of weight loss > 10% in the previous 6 months was 30 and 38% in patients diagnosed with gastric cancer, 26% in those diagnosed with pancreatic cancer and 10 to 15% in patients diagnosed with lung, colon or prostate cancer.

3. 3. 1. Cancer and Physical Fitness

Cancer and the associated treatments result in increased pain and fatigue, decreased cardiorespiratory fitness and decreased muscle mass and strength, which negatively impact on quality of life (48). As in CHF and COPD, there is an atrophy of type II skeletal muscle fibers (49) and a decreased oxidative capacity (50). The decreased cardiorespiratory fitness has been demonstrated in patients with breast cancer (51) and has been associated with reduced survival in lung and breast cancer patients (52, 53).

3. 3. 2. Impact of Physical Activity on Cancer

Several meta-analysis or systemic reviews demonstrate the positive impact of physical activity on cancer survivors, mostly in breast cancer patients (54-56). None of these studies looked specifically on the impact of physical activity in cachectic patients. The impacts of aerobic and anaerobic exercise, according to a meta-analysis including only randomized controlled trials of cancer survivors are (52):
- ↓ body weight in non malnourished breast cancer patients; no impact on lean mass
- ↑ peak oxygen consumption, peak power output, 6-min walk distance
- ↑ handgrip strength, bench press weight and leg press weight
- ↑ quality of life
- ↓ fatigue, depression

Physical activity during or after cancer treatment may also improve immune function, range of motion, chemotherapy tolerance, body image and mood, and may reduce number and intensity of treatment-induced side-effects and duration of hospitalisation (57).

3. 3. 3. Impact of Physical Activity and Nutrition on Cancer

Oral nutritional support improves calorie and protein intake of cancer patients who are malnourished or at risk of malnutrition but does not seem to increase weight, physical functioning, quality of life and survival (58). This raises the question of whether the addition of physical activity to nutritional support is more efficient than nutritional support alone.

One systematic review evaluated the interventions for fatigue and weight loss in adults with chronic illness (59). Regarding cancer patients, the authors reported that no studies evaluated quantitatively the impact of interventions for fatigue and weight loss. A recent meta-analysis also mentioned that so far no RCT explored the impact of physical exercise in cancer cachexia, although several studies on this topic are on-going in lung and head and neck cancer patients (60). Thus, presently the impact of physical activity combined with nutritional support has not been tested in cancer patients.
However, the American Cancer Society recently published a scientific report of expert opinions, in which they recognize the potential use of physical activity in underweight cancer survivors to reduce stress and increase strength and lean body mass (61). As physical activity increases energy expenditure, it may be essential to start concomitant nutritional support.

3. 3. 4. Contraindications of Physical Activity in Cancer

Contraindications to physical exercise in cancer are the same as in CHF and COPD. Several authors also raised concerns on the safety of physical activity in case of anemia, leucopenia, thrombopenia, lymphedema, cachexia and fatigue (62). Although no study has demonstrated a negative effect of physical exercise in these situations, Dimeo et al. suggest avoiding vigorous physical exercise at a platelet count < 20’000 µl and leucocyte count <1500/ µl (63).

The Australian Association for Exercise and Sport Science position stand, for instance, suggests avoiding: swimming and using public facilities in case of low absolute neutrophil count; high impact exercises or contact sports in case of low platelet counts or bone pain due to primary or metastatic bone cancer; exercises requiring balance and coordination in case of ataxia, dizziness or peripheral sensory neuropathy (57).

3. 3. 5. Recommendations of Physical Activity in Cancer

The recommendations for physical activity in cancer survivors are theoretically the same as those for the healthy population (Table 3) (48). However, the intensity of physical exercise has to be adapted to the peak heart rate or peak oxygen consumption, which is lower than in the healthy population. As a corollary, light activities (9-11 points on the Borg RPE) are perceived as moderate (8-14 on the Borg RPE) in cancer survivors (48). Furthermore, Bourke et al stretches that the characteristics of physical exercise have to be individualized in cancer patients as it is unlikely that they achieve the recommendations for healthy subjects (56). The Australian Association for Exercise and Sport Science position stand suggests the following recommendations for aerobic and resistance exercise during and after cancer treatment (57).
Table 6  
**Recommendations for patients with cancer (57)**

<table>
<thead>
<tr>
<th></th>
<th>Aerobic exercise</th>
<th>Resistance exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>3 to 5 days/wk</td>
<td>1-3 d/wk</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>50-75% of VO₂peak or HRR</td>
<td>50-80% 1-RM</td>
</tr>
<tr>
<td></td>
<td>11-14 on Borg RPE scale</td>
<td>Avoid high intensity in case of low hemoglobin levels, immunosuppression and fever</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>&gt;20 minutes/session</td>
<td>-</td>
</tr>
<tr>
<td><strong>Type</strong></td>
<td>Continuous</td>
<td>Concentric and eccentric using machine-weights, free weights, body weight and therabands</td>
</tr>
<tr>
<td><strong>Pattern</strong></td>
<td>-</td>
<td>1-4 sets, 6-10 repetitions</td>
</tr>
<tr>
<td><strong>Remark</strong></td>
<td>Deconditioned patients: Daily aerobic exercise, but lower intensity and shorter duration (e.g short bouts of 3-5 min with rest intervals). Slow progression Increase of duration before intensity</td>
<td>Deconditioned patients: Slow progression</td>
</tr>
</tbody>
</table>

VO₂ peak: highest VO₂ consumption on a particular exercise test.
HRR: heart rate reserve = difference between maximal heart rate and peak heart rate
Borg Rating of Perceived Exertion Scale (Borg RPE): score of 6 to 20, where 20 is maximal effort.

### 3. 4. Summary

Physical exercise positively affects physical fitness in diseases often related with cachexia as CHF, COPD and cancer. However, studies reporting on its impact in cachectic patients, in combination with nutritional support, are scarce or not existing. Consequently, recommendations of physical exercise may not be adapted to cachectic patients and should probably also include nutritional support.
5. References