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Effects of prehabilitation and rehabilitation including a home-based component on physical fitness, adherence, treatment tolerance, and recovery in patients with non-small cell lung cancer: A systematic review

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ABSTRACT

This systematic review aimed to examine physical fitness, adherence, treatment tolerance, and recovery for (p)rehabilitation including a home-based component for patients with non-small cell lung cancer (NSCLC). PRISMA and Cochrane guidelines were followed. Studies describing (home-based) prehabilitation or rehabilitation in patients with NSCLC were included from four databases (January 2000–April 2016, $N = 11$). Nine of ten rehabilitation studies and one prehabilitation study (437 NSCLC patients, mean age 59–72 years) showed significantly or clinically relevant improved physical fitness. Three (27%) assessed home-based training and eight (73%) combined training at home, inhospital (intramural) and/or at the physiotherapy practice/department (extramural). Six (55%) applied supervision of home-based

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components, and four (36%) a personalized training program. Adherence varied strongly (9–125% for exercises, 50–100% for patients). Treatment tolerance and recovery were heterogeneously reported. Although promising results of (p)rehabilitation for improving physical fitness were found (especially in case of supervision and personalization), adequately powered studies for home-based (p)rehabilitation are needed.

1. Introduction

Non-small cell lung cancer (NSCLC) concerns 85% of all lung cancer patients (Netherlands Cancer Registry, 2016a). Five-year survival rates remain low ranging from 55%, 41%, 13%, to 2% for stage I, II, III and IV, respectively (Netherlands Cancer Registry, 2016b). Standard curative treatments, including lung resection (Vansteenkiste et al., 2014) and concurrent chemoradiation (Eberhardt et al., 2015), lead to adverse events in ≥50% of patients and frequently require hospitalization (Janssen-Heijnen et al., 2004; Schild et al., 2003). High age (Netherlands Cancer Registry, 2016c), smoking-related comorbidities, frailty, poor performance status, and long-term physical inactivity are often present in patients with NSCLC (Janssen-Heijnen et al., 2004; Hsu et al., 2015; Semrau et al., 2014; Granger et al., 2014). These characteristics may affect mobility, independence, treatment tolerance, recovery, and prognosis (Gridelli et al., 2007; Cardenal et al., 2015; Glotzer et al., 2013; Kale et al., 2015; Hoogeboom et al., 2014). Resistance and endurance training can increase the functional and physiological reserve, thereby creating a safety margin to meet potential enlarged demands of cardiac output and other physical capacities at the time of disease and interventions (Hoogeboom et al., 2014; Carli and Zavorsky, 2005). Prehabilitation (therapeutic training before undergoing treatment) (Carli and Zavorsky, 2005) and rehabilitation (therapeutic training during and after treatment) (Spruit et al., 2013) can optimize physical fitness, treatment tolerance, recovery, and survival (Singh et al., 2013; Ni et al., 2016; Bade et al., 2015), even in older cancer patients (Chou et al., 2012; Jack et al., 2011; Kilari et al., 2016). However, intramural training (inhospital) or extramural training (at the physiotherapy practice or department) may counteract compliance of high-risk patients because of commuting problems, accessibility of services, multimorbidity, and vulnerability (Temel et al., 2009; Oosting et al., 2012). A personalized training program in a home-based setting might overcome these barriers and enhance both motivation and adherence, especially for vulnerable and older patients (Bade et al., 2015). Therefore, the aim of this study is to systematically review the literature regarding feasibility and effectiveness of prehabilitation and rehabilitation including a home-based component in patients with NSCLC by evaluating physical fitness, and to describe adherence and treatment tolerance, and recovery.

2. Methods

The Cochrane guidelines for systematic reviews (The Cochrane Collaboration, 2011) and PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (Moher et al., 2009) were followed. Databases Pubmed, Medline, Embase, and PEDro were searched for eligible articles describing patients with NSCLC undergoing prehabilitation or rehabilitation including a home-based component focusing on physical fitness (Table 1). Search terms were explored on free text words to avoid exclusion of recently published articles. Inclusion was limited to studies in English or Dutch language between January 1, 2000 and April 11, 2016. The primary outcome was physical fitness and secondary outcomes were patient adherence, exercise adherence, treatment tolerance, and recovery. Studies were excluded when insufficient training information was available to distinguish prehabilitation and rehabilitation, and when no physical intervention was applied.

2.1. Study selection

All search results were combined and duplicates removed. Assessment of title, abstract and full-texts according to eligibility criteria was performed independently by reviewers MP and ED. Inclusion of eligible studies was discussed until consensus. If no consensus was reached, a third person (BB) determined eligibility. Studies were included when full-text was available. Reference tracking was performed after full-text assessment in order to include additional relevant studies.

2.2. Data collection process and items

For each included article, the following information was independently collected, compared, and combined: first author, publication year, study type (prehabilitation/rehabilitation, country, type of study, randomization), demographics (number of patients with NSCLC, stage of disease, age, sex, treatment, comorbidity, performance status), description of the intervention (exercise content, frequency, intensity, measurement times, exercise time, follow-up, time of delivery, controls), and outcomes (physical fitness, patient adherence, exercise adherence, treatment tolerance, recovery). Physical exercises consisted of resistance and endurance training, and training effects were mainly evaluated by the 6-minute walk test (6MWT) distance. Results were described as mean ± standard deviation, mean (range), or mean difference ± standard deviation. A minimal clinically important gain of ≥42 m or 9.5% change was considered clinically relevant for 6MWT distance (Granger et al., 2015). Patient adherence was described; both patient and exercise adherence (percentage) were considered sufficient above 70%. Treatment tolerance and recovery were displayed by adverse events (numbers, including postoperative complications) and hospitalization time (days, mean ± standard deviation). Differences between outcomes were considered statistically significant if $P < 0.05$.

2.3. Qualitative and quantitative assessment

Methodological quality was independently assessed by using the domain-based evaluation for systematic reviews by the Cochrane 'Risk of bias tool' (Cochrane Statistical Methods Group and Cochrane Bias Methods Group, 2011a). Selection-, performance-, detection-, attrition-, and reporting bias were scored present (+) or absent (−). Low, moderate, or high risk of bias was determined by the percentage of present bias, corresponding to high (≤17%), moderate (18–33%), or low (≥50%) methodological quality, respectively. Therapeutic validity for quality of the training content was assessed by the CONTENT scale (Consensus on Therapeutic Exercise Training) (Hoogeboom et al., 2012; Herbert and Bø, 2005). Nine items regarding patient eligibility, competences and setting, rationale of the study, content of the study, and adherence were scored as performed (+) or not performed